

CLINICAL VIGNETTE

As a start to learning about the visual system, let's see how a visit goes in the eye clinic. We'll present a case to you exactly how it would present in the eye clinic. You may not know what all the terms mean or the significance of the findings until later in the module, but it will serve as a guide to help you see what is important clinically as we build the components of the visual system. We will refer back to the case later to show you how the patient's findings are explained by each segment as we discuss it. We have included a glossary at the end of this module to help you with the terminology, and to explain each term as we go.

PRESENTATION: EXAMPLE PATIENT

DU is a 38 year old woman with a known diagnosis of multiple sclerosis. She has had many symptoms in the past in her motor and peripheral sensory systems, but no known attacks in her visual system. She presents to the eye clinic with an urgent problem: decreased vision.

SYMPTOMS:**CHIEF COMPLAINT:**

- "My vision is bad to my right side."

SYMPTOM PURSUIT:

- First noticed this morning on awakening.
- No change from first notice till clinic exam (midafternoon)
- Vision on her right is "dim", not blurry, not blank. "Like looking through a very dense fog." Vision to the left side is normal, sharp, clear.
- Painless.
- First occurrence. Her pre-symptom vision was "20/20 in both eyes, without glasses."
- No double vision.
- Vision was good before this episode - has had frequent visits to neurologists for her other MS care, visual system often evaluated in these visits and was always "normal."
- Has covered each eye and tested vision monocularly - right side of vision in both eyes is lost, symmetrically.
- No flashing lights. No "window -shade" progression of symptomatic area.
- No other neurologic symptoms, "and I would know if I had them."
- No head trauma.
- No new medications.
- No change of symptoms in any field of gaze (i.e. same "dim area" whether looking right, left, up, down, or straight ahead.)

EXAMINATION:

- Visual Acuity: 20/20 right eye 20/20 left eye

Although she gets all the test letters correct, she has the sense that "some parts of the letters are missing to the right."

- Confrontation Visual Field testing:

Right gaze visual field of each eye symmetrically decreased to finger-counting stimulus testing. Defect does not cross vertical midline, but does cross horizontal midline of each eye's visual

field.

- Pupillary light reflexes:
 - 5 mm in dark, both eyes
 - 1 mm with flashlight, both eyes
 - Swinging flashlight test: no dilation of either pupil - no afferent defect.

Because her visual defects seem to be fairly “geographic”, you decide to map out exactly where she can and cannot see before you examine and dilate her eyes.

•VISUAL FIELD TESTS

Manual field testing shows marked constriction of her fields in both eyes. The right half of the field of each eye is nearly gone. There is perfect respect for the vertical meridian, and the left half of each eye’s field is entirely normal.

Computerized field testing shows that the right half of each eye is markedly reduced - the test light has to be made much brighter than normal for her to see it. The left half of each eye’s field is normal. There is respect for the vertical meridian.

In each testing method, there is a nearly perfect correspondence of the boundary of the loss between the right and left eyes. That is, the defect is homonymous.

PHYSICAL EXAMINATION OF THE EYEBALLS

- Lids, lashes: Normal
- Conjunctiva: No inflammation or dilation of normal blood vessels.
- Corneas: Clear, smooth, intact. No explanation for decreased vision.
- Anterior chambers: negative “volcano sign.” Normal depth, no inflammation.
- Irides: normal, round, all areas move briskly to constrict when light is shined in the pupils.
- Lenses: Clear, normal size and shape. No explanation for decreased vision.

AFTER DILATION OF IRIDES WITH EYE DROPS:

- Vitreous humor/cavities: Clear, normal. No blood, no inflammation.
- Retina:
 - All areas attached, “flat” to choroid. No tears, no tumors, normal curvature.
 - Blood vessels: normal caliber. No bleeding. No ischemia. No neovascularization.
 - Pigment in fovea and periphery normal. Color normal.
- Optic nerve:
 - No swelling.
 - Normal cupping.
 - No hemorrhages.
 - Margins sharp.
 - Nerve tissue normal color, no pallor.

SUMMARY:

Right homonymous visual field loss, respecting vertical midline, with completely normal physical exam, pupillary light reflex, and visual acuity.

The data in this kind of case, and the terminology, might seem overwhelming. But in the next few chapters, you will learn all of this terminology and understand enough of the visual system to be able to localize this lesion and speculate what will be seen on her brain imaging studies.

Let’s get started on getting the pieces of this puzzle assembled!

VISION

All of the color, shape, texture, depth, and movement you see in the world, and all of the words in this syllabus, are brought to you by your visual system. Photons of light entering the eye convey information about the world to the brain by means of the neurons in the visual pathways, starting at the eye.

It is often useful to compare the eye to another visual device, the camera. We can broadly divide the operations of a camera into two parts: 1) the imaging/optical apparatus of the camera, which focuses the visual image, and 2) the film/digital array, which captures the image (that will be sent elsewhere for processing). The eye has optical apparatus (the cornea and lens) that focuses the visual image, and it has the retina, which is analogous to the film. The visual cortex serves as the photoprocessor and interpreter of the images.

In the first part of the Vision module, Dr. Uhlrich will discuss:

- the fundamental parts of the eye
- optics of the eye and the underlying neural control
- how the retina processes the visual image
- the central visual neural pathways that further analyze the visual information

In the second part of the Vision module, Dr. Heatley will discuss:

- common clinical tests of visual function
- predominant clinical issues and diseases affecting vision.

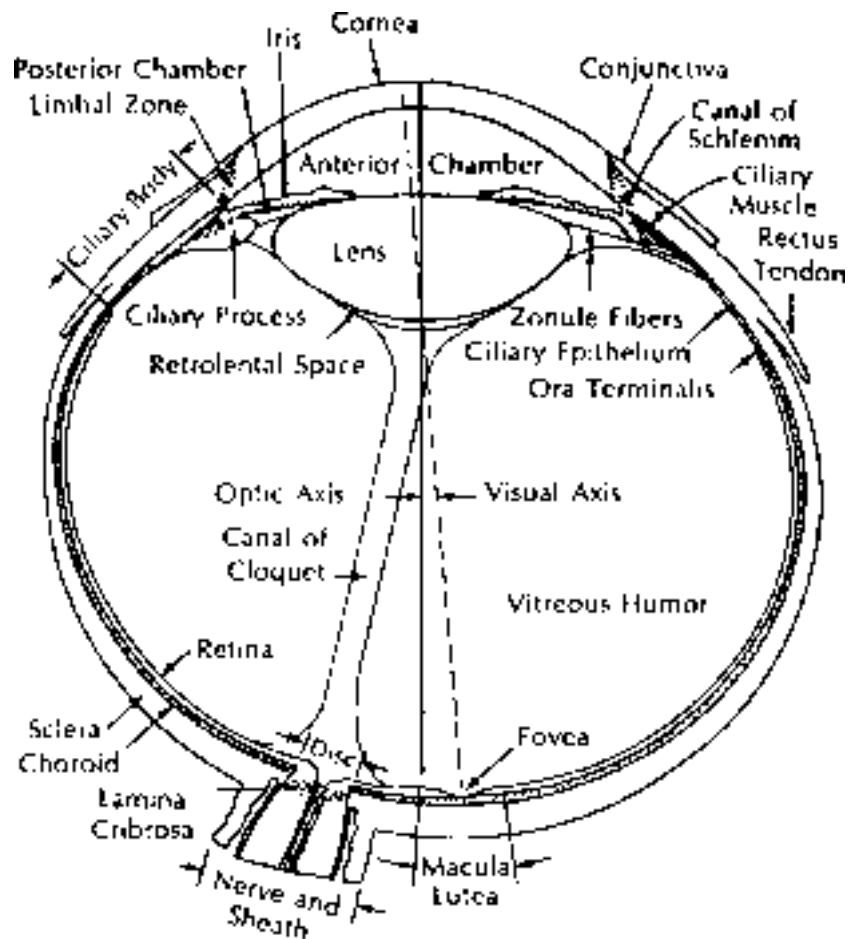
So, let's turn on the light and see what happens.

GROSS STRUCTURE OF THE EYE

The gross structure of the eye should look familiar from gross anatomy.

The **sclera** and **cornea** are continuous and make up the strong outer shell of the eye. The sclera is made up of cross-linked collagen fibers, which render the tough indistensible character. Posteriorly, the sclera is contiguous with the sheath of the optic nerve, which continues into the cranium as the dura mater.

Horizontal section through the human eye. The eyeball is a sphere about 2.5 cm in diameter that is fronted by a transparent, bulging cornea. The eye is contained in the cavity of the orbit where it is embedded in a thick layer of fascia, fat, and the extraocular muscles.



Cross section of the human eye (From Walls 1942)

STRUCTURES IN THE OPTICAL PATH

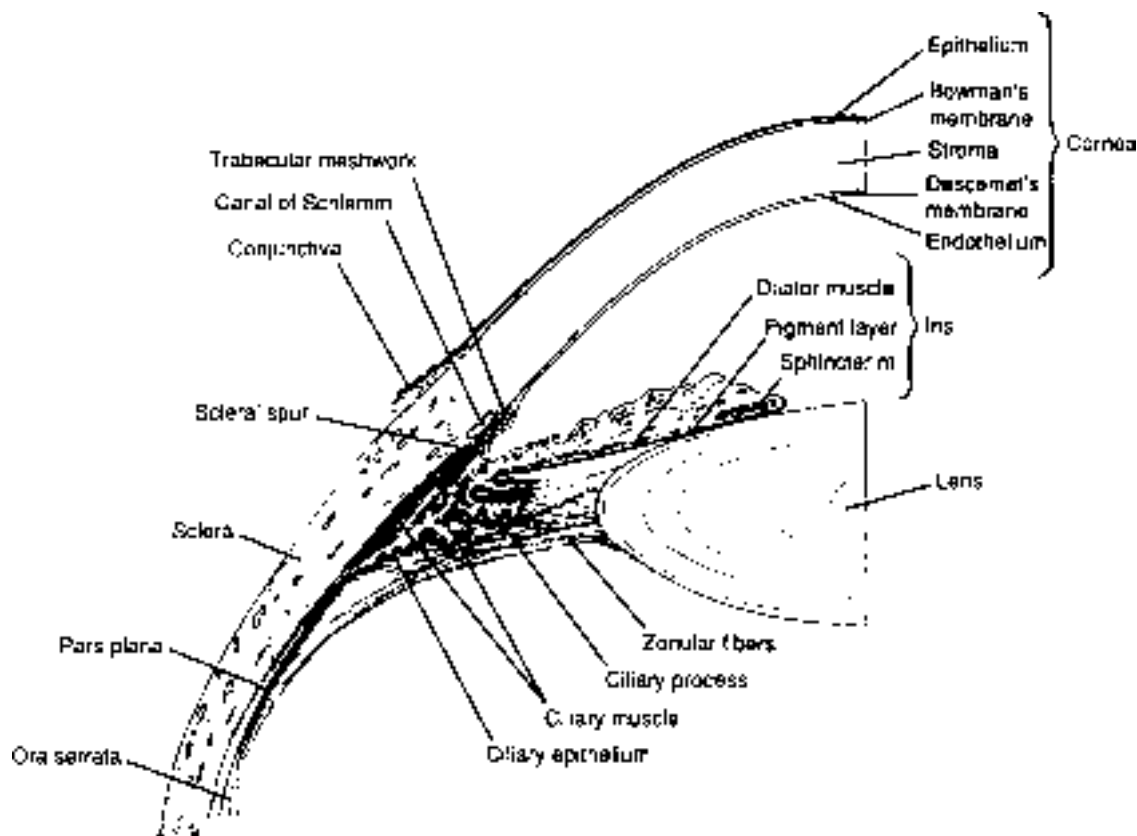
Light passes through a number of important structures while passing from the anterior to the posterior of the eye. The optical structures that we will be examining in detail, in order, are:

- The **cornea**, the first structure that light encounters when it impinges on the eye. Anteriorly in the eye, the collagen fibers of the sclera become regular in orientation and tightly packed, thus forming the transparent cornea through which light passes. Essentially, the cornea is specialized, transparent sclera. The integrity of the cornea depends on the layer of tear fluid that covers it externally. The cornea is the major refractor (bender) of light in the eye. (The cornea is not under neural control.)
- The **pupil**, actually a hole in the middle of the muscles of the colored **iris**. The iris is a diaphragm under neural control.
- the **lens**, a crystalline structure that changes shape to change the refractive power of the eye. The shape of the lens is under neural control.
- the **retina**, the multi-layered neural structure in which photons of light are transduced by receptors into a neural signal and neural processing begins.

CHAMBERS IN THE OPTICAL PATH

Light passes through three fluid-filled cavities, or chambers, in the eye while passing from front to back.

- The **anterior chamber** is the space between the cornea and the iris. It is continuous, via the pupil, with the **posterior chamber**, which is the area between the iris and the lens.
- The anterior and posterior chambers are filled with **aqueous humor**, a clear fluid that provides nourishment and immunocomponents to the avascular cornea and lens. Aqueous humor also provides a positive fluid pressure to maintain the inflated shape of the eye. Aqueous fluid is produced by the **ciliary body** at the lateral edge of the posterior chamber. The ciliary body consists of the aqueous-producing epithelium of the ciliary processes as well as the ciliary muscle. Aqueous flows anteriorly through the pupil into the anterior chamber, where much of it is resorbed by passing through the **trabecular meshwork** and the **Canal of Schlemm** into the aqueous veins of the sclera. If there is obstruction of drainage of aqueous humor out of the eye, intraocular pressure can increase significantly and fatally injure neurons in the retina. Dr. Heatley will discuss this in regard to



Anterior chamber angle and surrounding structures.

glaucoma later in this module.

- the **vitreal chamber** is the region from the posterior side of the lens to the retina. This comprises about 80% of the volume of the eye. The vitreal chamber is filled with transparent **vitreal humor**, a thick, hydrated network of collagen fibers (like jelly) that helps support the fragile retina.

GROSS STRUCTURE OF THE EYE: PRACTICE QUESTIONS

1. Which of the following statements about the organization of the eye is **TRUE**?
 - A. light impinging on the eye first encounters the lens
 - B. the pupil is situated directly behind (posterior to) the lens
 - C. the largest chamber in the eye is the posterior chamber, which is located directly in front of the retina
 - D. these structures are contiguous: cornea, sclera, optic nerve sheath, dura mater of the cranium
 - E. the shape of the cornea is under neural control

2. Which of the following statements about fluids in the eye is **TRUE**?
 - A. the cells of the retina are nourished by the aqueous humor
 - B. the aqueous humor is transparent, while the vitreous humor is opaque
 - C. the aqueous humor is produced by the ciliary body and reabsorbed through the trabecular meshwork.
 - D. the aqueous humor is thicker (more gelatinous) than the vitreous humor
 - E. the posterior chamber is filled with vitreous humor

GROSS STRUCTURE OF THE EYE PRACTICE QUESTIONS: ANSWERS

1. D
2. C

IMAGE FORMATION: OPTICS, THE LENS AND ACCOMMODATION

Optics are what's important in the earliest stages of the visual pathways. Ideally, the optics of the eye are designed so that a visual image focuses sharply on the retina.

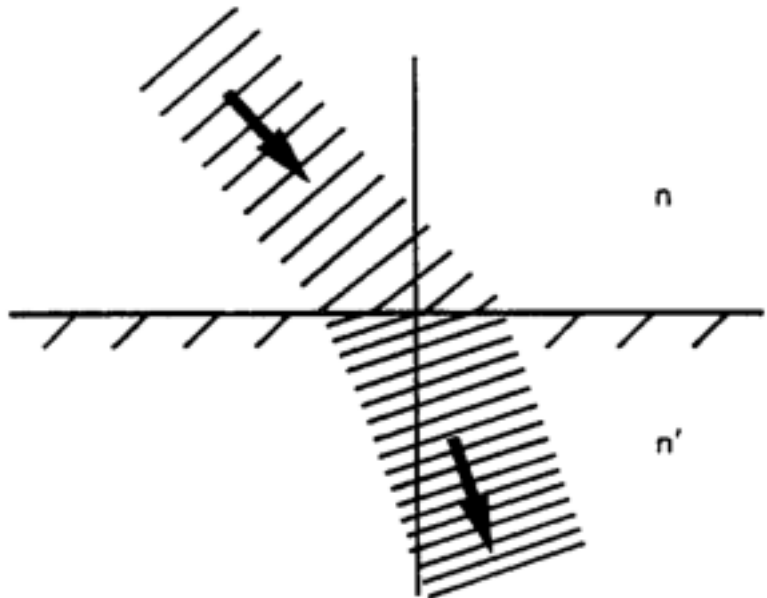
The visual image is focused by refraction (or bending) of light rays as they pass through the anterior (front) of the eye. The major refractors are the cornea and the crystalline lens. The cornea is more powerful. The *principal refraction occurs at the air-tear interface on the surface of the cornea*. However, the lens is also important because it changes shape, which alters and fine tunes the focus of the eye. So, our ability to change our focus from distant to near objects and back again depends on the flexibility of the lens. (And, this is vital to first year medical students because the shape of the lens is under neural control.)

Principles of Refraction (from your college physics course)

Light is bent at the interface between any two materials of differing densities (or more accurately, differing indices of refraction). When going from a less dense to a more dense material, light is bent towards the normal line/surface. The amount of *bending is proportional to the difference in density between the two materials*.

The index of refraction of air is, by definition, 1.000. The tissues of the eye have the following indices of refraction:

Air	1.000
Tears	1.336
Cornea	1.376
Aqueous	1.336
Lens	1.410
Vitreous	1.336



Light (following the arrows in the figure) is bent towards the normal line (an imaginary line drawn perpendicular to the surface interface) as the light passes from a less dense medium (n) to a more dense medium (n').

Comparing the indices of refraction, you can see that the surface with the greatest difference in refractive index is the air-tear interface. The curvature of a surface is also important, and the lens can increase in curvature to increase refraction. But when all the variables are factored in, *the greatest amount of refraction is done at the air-tear interface on the surface of the cornea*. The importance of this interface is easily appreciated by opening your eyes under water, which has a refractive index similar to that of tear film. The water-tear interface virtually eliminates the refraction that normally occurs at the air-tear interface, and the resulting visual image is blurred.

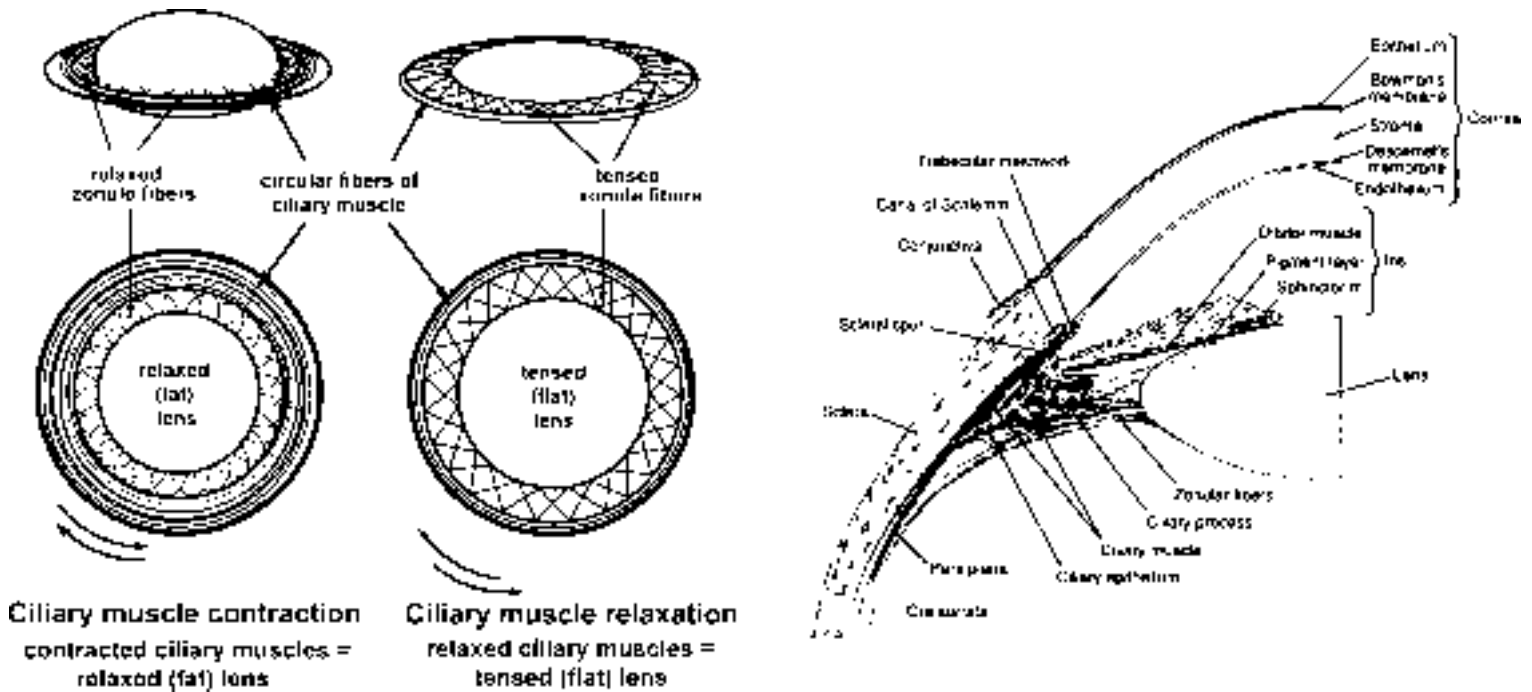
THE LENS AND ASSOCIATED STRUCTURES

The lens of the eye, about the size of an M&M candy, is purely ectodermal in origin. It has no blood supply and depends on nutrients from the aqueous humor. The lens is built from relatively moldable material. The lens is surrounded by a transparent lens capsule to which are attached the **zonule fibers**. The zonule fibers suspend the lens from the more peripherally-located **ciliary body**. The ciliary body encircles and essentially connects with the inner aspect of the globe of the eye. The bulk of the ciliary body is consists of bundles of muscles.

FUNCTION OF THE LENS

Distance vision

The normal eye is constructed so that distant images are focused clearly on the retina. The lens capsule is *normally* under tension due to the elastic tissue that supports the ciliary muscle. Thus, the lens “wants” to round up. However, the tension of the zonule fibers when the eye is focused on distant images pulls the lens relatively flat. The flat lens, in combination with the other optical structures of the eye, brings light from objects about 20 ft distant or greater into focus on the retina. At the same time, objects that are closer than 20 feet away are *out* of focus on the retina. So, when the ciliary muscle is released and the lens is flat the normal eye is focused optimally for distance vision.



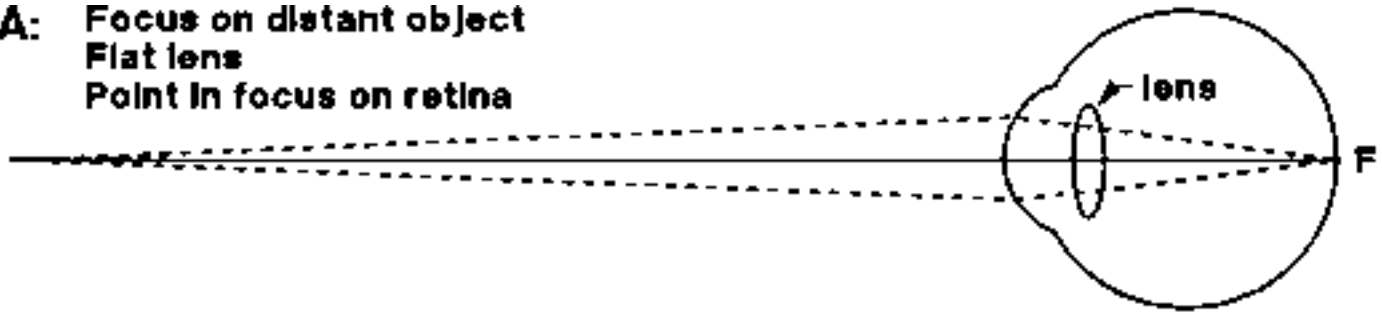
Near vision

The ciliary muscles in the ciliary body are at rest for distance vision, but they must contract for near vision (viewing a near object). As the ciliary muscles contract, they pull the ciliary body toward the lens, and the tension exerted by the zonule fibers on the lens relaxes, and the intrinsic elastic properties of the lens allow it to round up. As mentioned earlier, the lens is fairly elastic and

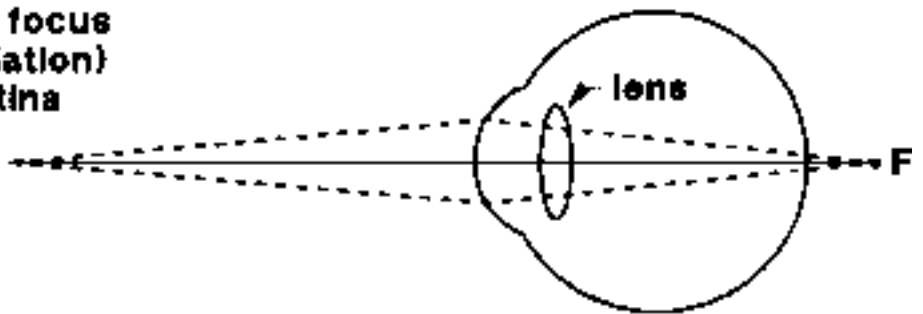
rounded when *it* is not under tension. This increased curvature increases the refractive power of the lens and shortens its focal length, thereby bringing closer objects into focus and defocusing the more distant objects. The *process by which we can alter the shape, and therefore the refractive power of the lens to focus on a closer object* is known as **accommodation**. Accommodation increases the refractive power of the lens through the action of the ciliary muscles.

The effect of accommodation of the lens on focus. When the ciliary muscles are relaxed, the zonule fibers are taut, the lens is flat, and distant objects are in focus (F) on the retina (A). In this state, near objects are out of focus (B). During accommodation (C), the lens fattens up, thereby bending the light more, and brings the nearer object into focus on the retina.

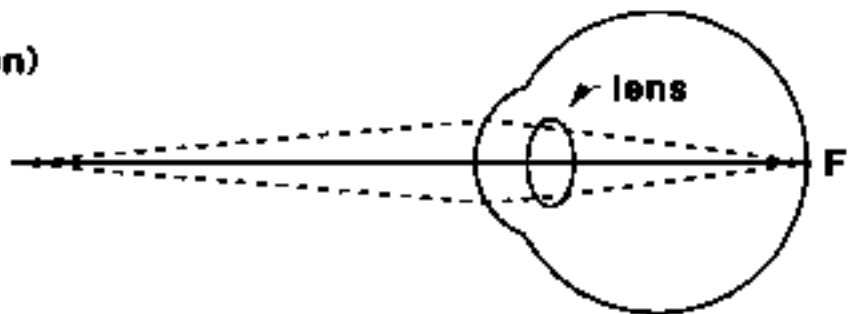
A: Focus on distant object
Flat lens
Point in focus on retina



B: Near object, but distant focus
Flat lens (no accommodation)
Point in focus behind retina
Blurred image on retina



C: Focus on near object
Fat lens (accommodation)
Point in focus on retina



How does ciliary muscle contraction reduce tension on the zonule fibers?

It may seem improbable that contraction of the ciliary muscle *reduces* tension on the zonule fibers, but the action is easy to understand from the anatomy of the ciliary muscle. The zonule fibers are attached to the ciliary muscle, which forms a ring around the lens. The circular muscle fibers of the ciliary muscle encircle the lens like a sphincter. When the circular muscle fibers contract, the diameter of the ring of attachment of the zonule fibers decreases, and the tension on the zonule fibers is relieved.

A second set of ciliary muscle fibers also assist. The *radial fibers* have their origin on a region of the sclera (the scleral spur) and insert near the outer fixation point of the zonule fibers. As the radial ciliary muscles contract, they pull the attachment of the zonule fibers forward, which reduces the diameter of the ring of attachment and reduces the tension on the zonule fibers.

Accommodation, then, depends upon two factors: 1) contraction of the ciliary muscles, and 2) the capacity of the lens to assume a more convex shape when tension on the zonule fibers is reduced.

INNERVATION OF THE CILIARY MUSCLES

Neural innervation of the ciliary muscles is primarily under **parasympathetic control**. The ciliary muscle does receive some sympathetic innervation, which opposes the parasympathetic action. However, this sympathetic input is minor. The most potent means of controlling lens shape is through increasing or decreasing the parasympathetic input.

The Parasympathetic Pathway:

- parasympathetic preganglionic neurons in Edinger-Westphal nucleus
axons travel in the oculomotor nerve
- postganglionic neurons in the ciliary ganglion,
axons travel in the ciliary nerve

PROBLEMS WITH LENS FUNCTION

You've read that when the ciliary muscles are relaxed in the optically ideal eye, the lens is flat and distant objects are in focus, and then the lens fattens up through accommodation to bring nearer objects into focus. However, not all eyes act ideally.

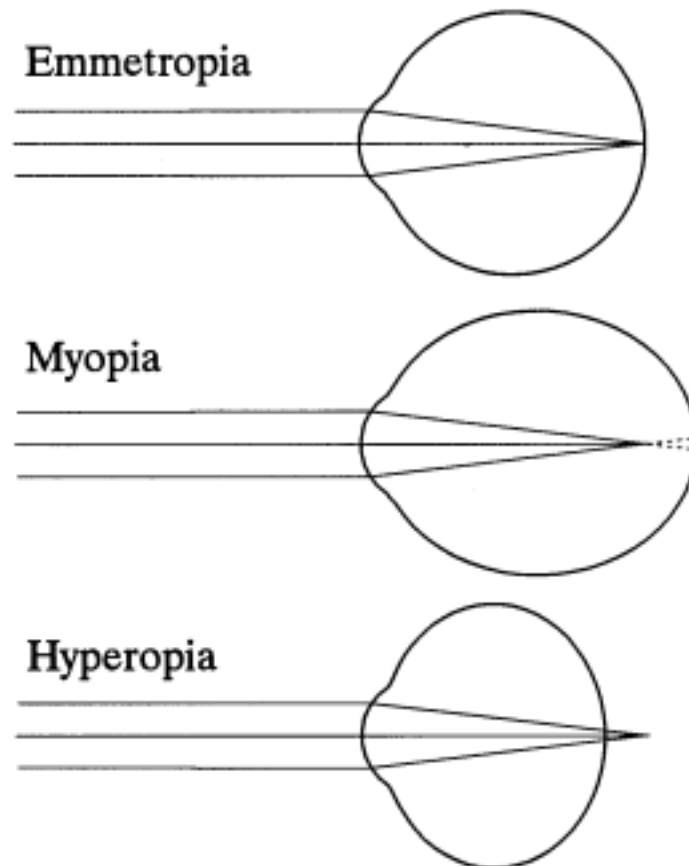
There is a progressive loss in the elasticity of the lens and in the capacity of the ciliary muscles as we age, which leads to a progressive decrease in our ability to accommodate. This is called **presbyopia** (G. *presbys*, old man + *ops*, eye). This decrease in accommodative capacity begins practically at birth, but does not become noticeable until it begins to interfere with reading, usually around age 45 years old. Then, we all go to see Dr. Heatley and his colleagues to get "reading glasses," which provide added refractive power to compensate for the inability of the lens to fatten up.

Also with increasing age, opacities in the lens can appear. These opacities are termed **cataracts** and they can adversely affect the optical quality of the eye. Dr. Heatley will discuss cataracts in more detail.

REFRACTIVE ERRORS

A distant image is perfectly focused on the retina under ideal optical conditions. This is called **emmetropia** (G. *emmetros*, according to measure). Sadly, such eyes are rare. For example, many of us require glasses long, long before we reach age 45. Discrepancies between the eye and its optics cause the majority of the human population to have some form of refractive error. Refractive problems arise from *a mismatch between the refractive power of the lens and the size of the eye*.

We categorize the refractive ability of an eye according to its imaging of distant objects (defined as being 20 or more feet away) when the ciliary muscle is relaxed (i.e., the lens is flattened = no accommodation). For all practical purposes, the rays of light from an object at such a distance are in parallel when they reach the eye.



Refractive errors

People who cannot bring distant objects into clear focus are said to be myopic. **Myopia** is caused by the cornea being too curved or the eyeball being too long on the anterior-posterior axis. In either case, with the lens as flat as it can be, the image of the distant object is focused *in front of* (anterior to), rather than on, the retina. The light rays from the distant object are refracted too much and create a blurry image.

However, since additional refraction is normally required to bring nearer objects into focus, the myopic eye is seemingly pre-set for focusing near objects. The myopic eye can see near by objects quite well since the optics of the eye focus the image of nearby objects sharply on the retina. Thus, people with myopia are referred to as nearsighted.

Some individuals have optic that seemingly do the opposite. People who can focus the image of distant objects on their retina, but not near objects, are said to be hyperopic. In contrast to myopia, **hyperopia** is caused by the refractive power of the eye being too weak, or by the eyeball being too short. So, the image of a distant object is actually in focus *behind* (posterior to) the retina. The eye must accommodate to bring the image of distant objects into focus sharply on the retina, and it can do this pretty well. However, the eye cannot accommodate any more to bring near objects into focus (which you now know requires additional accommodation). So, distant objects look sharp, but nearby objects look blurry. Thus, people with hyperopia are referred to as farsighted. Driving with hyperopia can be OK, but reading is literally a headache. The headache comes from fatigue of the ciliary muscle as it is constantly stimulated to maximally contract to see the near image.

**IMAGE FORMATION: OPTICS, LENS AND ACCOMMODATION:
PRACTICE QUESTIONS**

1. Which of the following pairs is **INCORRECT**?
 - A. emmetropia — distant image focused sharply on retina without accommodation
 - B. myopia — eye is too long for its refractive power
 - C. presbyopia — stiffening of the lens with age, leading to inability focus distant objects
 - D. hyperopia — eye is too short for its refractive power
 - E. dopia — refractive capability of one of Snow White's seven dwarfs

2. Which of the following statements related to the lens is **TRUE**?
 - A. the primary innervation of the ciliary muscles comes from the sympathetic pathway
 - B. most of the refraction of light is accomplished by the lens
 - C. when the ciliary muscle contracts, the lens is put under tension and flattens
 - D. accommodation is the process wherein the lens increases in curvature to bring near objects into focus on the retina
 - E. when not under tension, the lens assumes a flattened shape

3. What type of lens would you prescribe for a hyperopic patient?
 - A. a convex (or 'plus') lens, which bends the light rays toward each other
 - B. a concave (or 'minus') lens, which diverges the rays of light
 - C. don't prescribe a lens; have the patient sit in the back of the room and squint
 - D. colored contact lenses
 - E. none of the above

**PRACTICE QUESTION ANSWERS — IMAGE FORMATION: OPTICS,
LENS AND ACCOMMODATION**

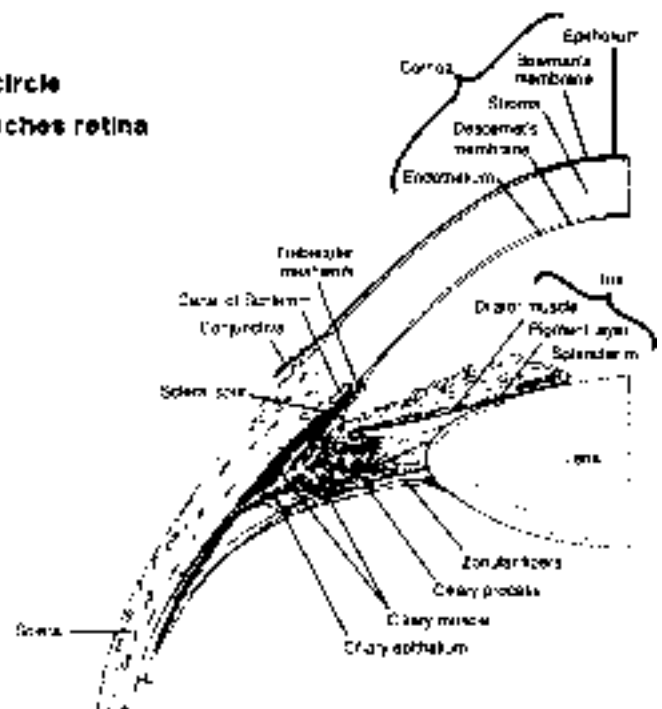
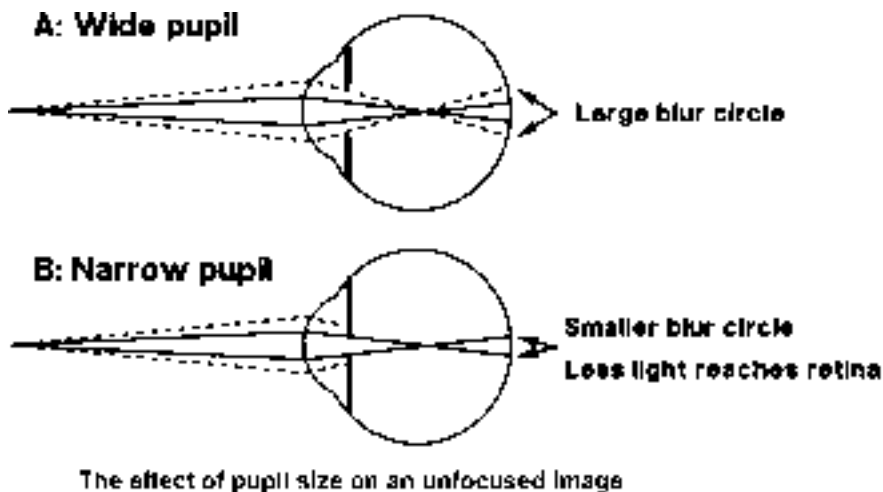
1. C; yes, the lens stiffens, but this prevents the accommodation to focus on *near* objects. During this lecture, ask if you can look in my eyes!!!
2. D
3. Answer “A” is correct. Great job if you figured this out. In hyperopia, the image is focused behind the retina, so bending the light more with a convex lens would move the focused image forward onto the retina. Answer “C” might work, but it’s time to work on your doctor-patient skills.

IMAGE FORMATION: THE IRIS AND PUPIL

FUNCTIONS OF THE PUPIL

The amount of light reaching the retina is controlled by variations in the size of the **pupil**, the hole or aperture of the **iris**. The pupil serves two important functions:

- First, the diameter of a normal human pupil can vary enormously, from less than 2 mm in diameter in very bright conditions (e.g., walking outside on a blindingly bright, sunny day after a snow storm) to more than 8 mm in diameter in complete darkness. Since the area of a circle is proportional to the square of its radius (area = πr^2), this represents a 16 fold change in pupil area ($8^2/2^2 = 64/4 = 16/1$). We take for granted that our pupils widen in the dark to let in more light and constrict in the light. Varying the size of the pupil is one method by which the eye adjusts and continues to function well across the wide range and variations in the intensity of illumination that we encounter in life.
- Second, constriction of the pupil increases the crispness of unfocused retinal images by reducing the stray light that contributes to the blur. Even though an image is not in perfect focus on the retina, the image is much sharper, more like the original point source, when the pupil is small. More of the light comes in parallel rays, rather than stray light entering at odd angles. The small pupil also *increases the depth of field* of the eye because it decreases the amount of blur of objects that are

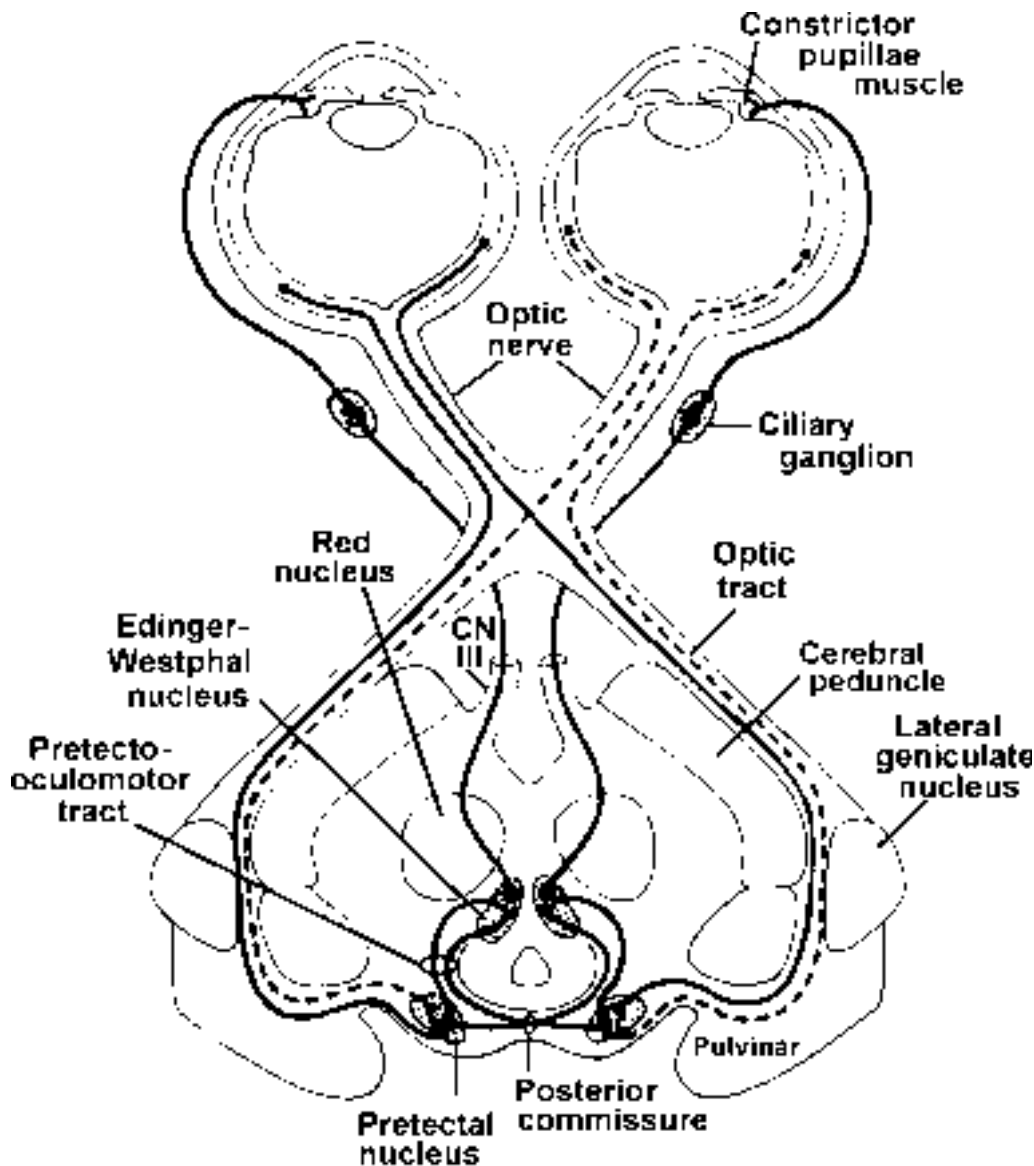


closer or farther away from the point of focus. The same things happen when you increase the F-number (or F-stop) of a camera by decreasing the aperture size. Those of you who require corrective lenses can test this by removing your glasses and looking through a pinhole. Objects will appear clearer. However, the images will also be darker because more light is blocked.

INNERVATION OF THE IRIS

The iris contains two muscles, the constrictor pupillae muscle and the dilator pupillae muscle, and it receives both parasympathetic and sympathetic innervation.

- **Constriction of the pupil (miosis)** is accomplished by contraction of the circular **constrictor pupillae muscle** as a result of **parasympathetic** innervation.



The pupillary light reflex, resulting in pupillary constriction
(from Williams and Wilkins, 1969).

The *afferent* (*sensory*) portion of the pupillary light reflex conveys information about changes in light level from the eye to the pretectal nuclei. The pretectal nuclei project to the Edinger-Westphal nucleus (near the oculomotor nucleus in the brain stem).

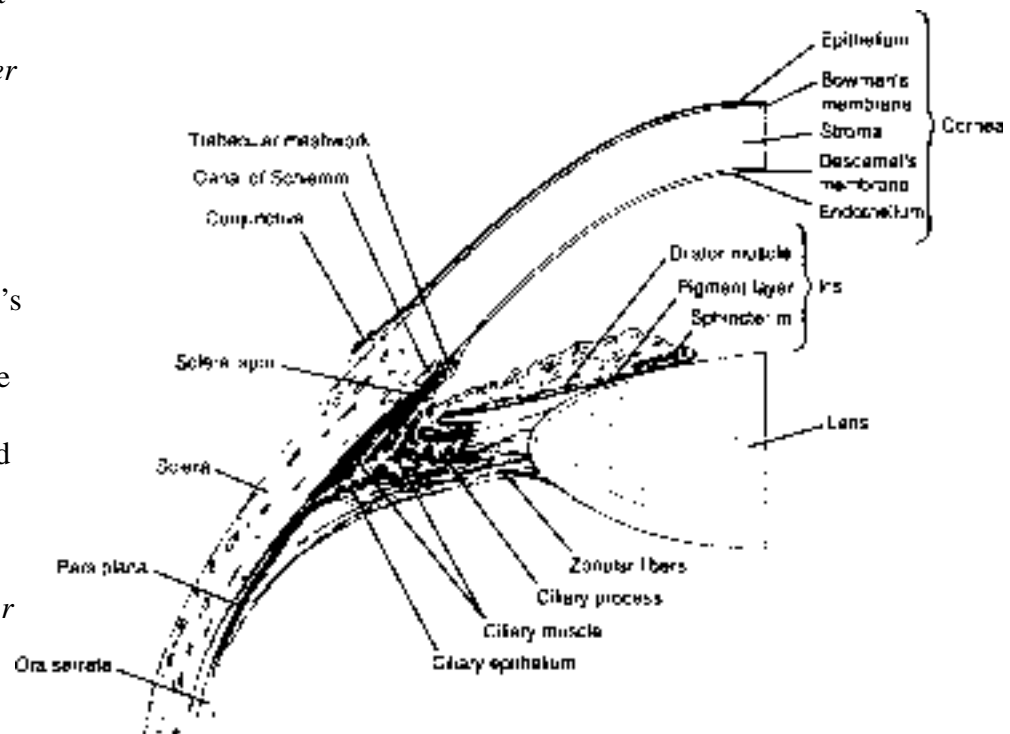
In the *efferent* (*motor*) portion of the pupillary light pathway, neurons in the Edinger-Westphal nucleus project via the oculomotor nerve to the ciliary ganglion, which projects to the constrictor pupillae muscle in the eye. Disruption of this pathway results in dilation of the pupil, because the dilator pupillae muscle is then un-opposed (coming up soon).

Notice that the circuit is highly redundant, with overlapping and crossing paths. Retinal ganglion cell axons project *bilaterally* to the pretectal region, just rostral to the superior colliculus, and the pretectal cells project *bilaterally* to each other and to the Edinger-Westphal nucleus. The result of these bilateral projections is that each eye can initiate a pupillary response for itself (**the direct light reflex**) and for the other eye (**the consensual response**)!

Pupillary abnormalities are important clinical signs

Important point: *The direct pupillary light reflex of one eye is accompanied normally by the same response in the opposite eye, even if the opposite eye is not stimulated by light.* So, failure or reduction of pupil constriction in either eye can be an important clinically. Dr. Heatley will discuss in detail clinical uses of the pupillary light reflex. For now, note that you can distinguish optic nerve lesions from oculomotor lesions using the pupils. Here's how.

If the optic nerve of one eye is damaged, that eye's pupil will not constrict when light is shown into it (no direct response), but it *will* constrict when the *other* eye is illuminated (a consensual response). If, instead, the oculomotor nerve or nucleus of one eye is damaged, then that eye's pupil cannot constrict under *any* circumstance (no direct response). However, a light shined into that eye (with the damaged motor path) will still produce constriction in the *other* eye (a consensual response).



Anterior chamber angle and surrounding structures.

Linkage between Accommodation and Pupillary Constriction

The parasympathetic innervation of the iris sphincter pupillae muscles is similar to that of the ciliary muscles controlling accommodation. In fact, the actions of pupillary constriction and accommodation of the lens are commonly related and comprise two of the three components of the **near response**. The near response occurs when gaze is shifted from a distant object to a near object. The third component of the near response is convergence, the nasalward rotation of the two eyes. So, in the near response, the lens fattens, the pupils constrict, and the eyes turn in. The neural pathways responsible for the linkage of the components of the near response are not clear.

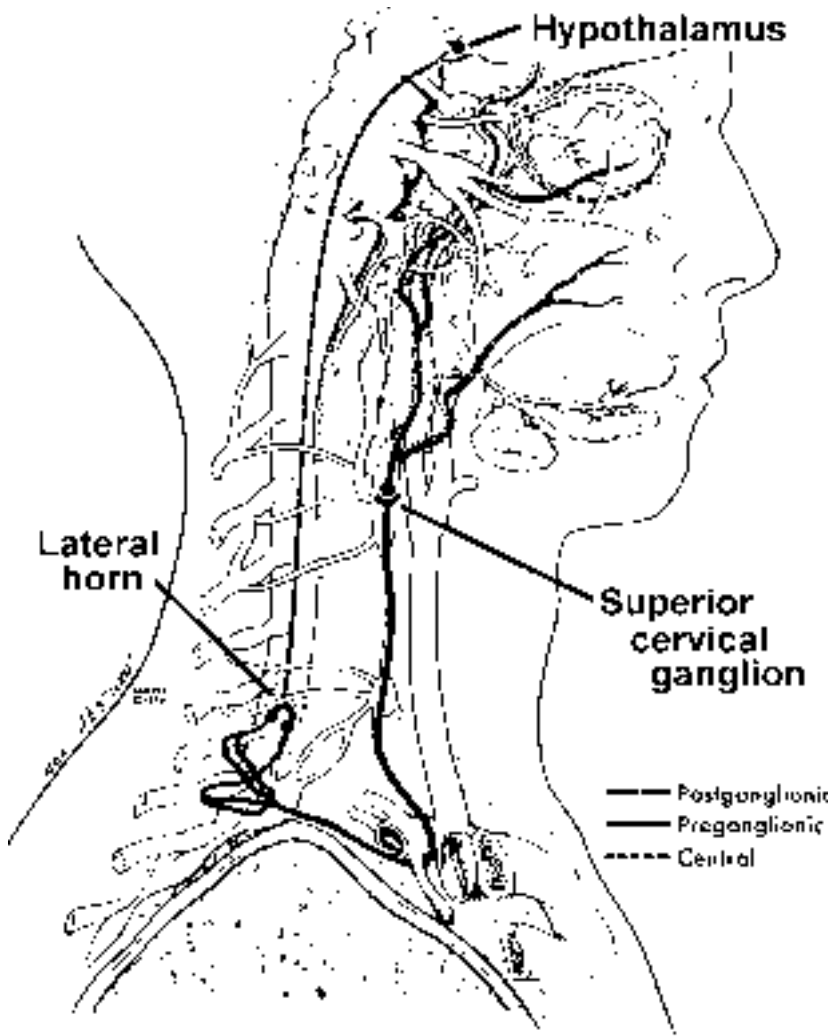
Clinical note: It is possible to dissociate the pupillary light response from the pupillary constriction seen during the near response in some patients with neurological damage. For example, in patients with CNS syphilis, the direct and consensual pupillary constriction with light may be reduced or lost, while the pupillary constriction that accompanies accommodation and convergence is preserved. This is called the Argyll-Robertson pupil. The precise location of the lesion is not known, but the best guess is in the pretectum.

- **Dilation of the pupil (mydriasis)** is accomplished by contraction of the **dilator pupillae muscle**, which receives **sympathetic** innervation through a circuitous pathway.

Dr. Harting discussed sympathetic innervation of the eye in his spinal cord and brainstem lectures. Here's a summary:

Sympathetic fibers emerge from the hypothalamus and descend through the brainstem (some axons synapse here, others do not) to the lateral horn of the spinal cord where they synapse on preganglionic cells. The axons of the preganglionic cells exit the spinal cord about T1 via the ventral roots and ascend to the superior cervical ganglion. Postganglionic cell axons from neurons in the superior cervical ganglion travel along with the carotid artery and then with the ophthalmic arteries, over the ciliary ganglion (but do not synapse here), and finally, in the long root of the nasociliary nerve to the dilator pupillae muscle in the eye.

Disruption of this pathway (anywhere along its course!) results in constriction of the pupil, because the constrictor pupillae muscle is then un-opposed. **Ptosis** (drooping) of the eyelid also occurs because this sympathetic pathway also innervates **Mueller's muscle** (superior tarsal), a smooth muscle that helps to open the upper eyelid (remember Horner's Syndrome = ptosis, miosis and anhidrosis).



Sympathetic innervation of the eye (from Maloney et al. 1980).

PHARMACOLOGY OF THE IRIS

The sympathetic and parasympathetic systems are both tonically active and continuously influencing the size of the pupil. The size of the pupil reflects the relative balance between the two systems. The pupil is constricted either by exciting the parasympathetic system, or by inhibiting the sympathetic system. Alternatively, as you've probably guessed, the pupil is dilated by exciting the sympathetic system, or by inhibiting the parasympathetic system.

The parasympathetic and sympathetic inputs to the iris use different neurotransmitters at the neuromuscular junction:

- **parasympathetic system (*constricts*): cholinergic**
- **sympathetic system (*dilates*): noradrenergic**

As a result, the size of the pupil can be manipulated pharmacologically:

- **Miotic agents**, which cause constriction of the pupil (**miosis**), are either cholinergic agonists (e.g., pilocarpine, carbachol) or noradrenergic antagonists (e.g., phentolamine).
- **Mydriatic agents**, which cause dilation of the pupil (**mydriasis**), are either noradrenergic agonists (e.g., epinephrine, phenylephrine, cocaine) or cholinergic antagonists (e.g., atropine, tropicamide).

Trace the pathway underlying the pupillary light reflex for light shined in one eye. That is, one optic nerve (Level 18); optic chiasm (Level 17); bilateral optic tract (Levels 16-12); bypassing the LGB (level 12); pretectum and posterior commissure (Level 11); to Edinger-Westphal and C.N. III root (Level 10).

Level 16



Level 13



Level 10



Level 17



Level 14



Level 11



Level 18



Level 15



Level 12



PRACTICE QUESTIONS — IMAGE FORMATION: THE IRIS AND PUPIL

1. Which of the following is **NOT** an advantage of having a constricted pupil?
 - A. increased depth of field
 - B. increased sensitivity in the dark
 - C. unfocused images are sharper on the retina
 - D. helps to protect the eye from intense light
 - E. none of the above

2. Both pupils of Mitsy and the dog Bitsy are dilated, even in daylight. Mitsy and Bitsy claim that they were simply drawn that way. Which of the following is also possible?
 - A. Mitsy and Bitsy are focusing on a near object, and their dilated pupils are part of the near response
 - B. Mitsy and Bitsy have a domineering parasympathetic system
 - C. Mitsy and Bitsy have bilateral lesions of the descending sympathetic fibers in the brainstem
 - D. Mitsy and Bitsy have ingested a noradrenergic agonist
 - E. two of the above



3. Which of the following will result in the *complete* loss of pupillary constriction in the right eye when light is directed in the left eye?
 - A. lesion of the left Edinger-Westphal nucleus
 - B. lesions of the right optic nerve and left optic tract
 - C. lesion of the right oculomotor nerve
 - D. lesion of the posterior commissure
 - E. two answers are correct

4. Let's try another one. After which of the following lesions will you still observe bilateral constriction of the pupils when light is shined in the right eye?
- A. a lesion of the right optic tract
 - B. a lesion of the posterior commissure and the left pretectum
 - C. a lesion of the left ciliary ganglion
 - D. bilateral lesions of primary visual cortex (think about it!)
 - E. two answers are correct
5. Let's put the lens and pupil together. Which of the following results from activation of the parasympathetic innervation of the eye?
- A. distant objects will come into sharp focus
 - B. the ciliary muscles will contract and *flatten* the lens
 - C. more light will reach the retina
 - D. the dilator pupillae muscles will contract
 - E. miosis

PRACTICE QUESTION ANSWERS — IMAGE FORMATION: THE IRIS AND PUPIL

- 1. B
- 2. D — Remember to ask me about “belladonna” during this lecture.
- 3. C
- 4. E (A and D) — Note that the pupillary reflex is a “subcortical” pathway. Subcortically-mediated visual reflexes/functions are maintained, even with large cortical lesions.
- 5. E

RETINAL STRUCTURE AND FUNCTION

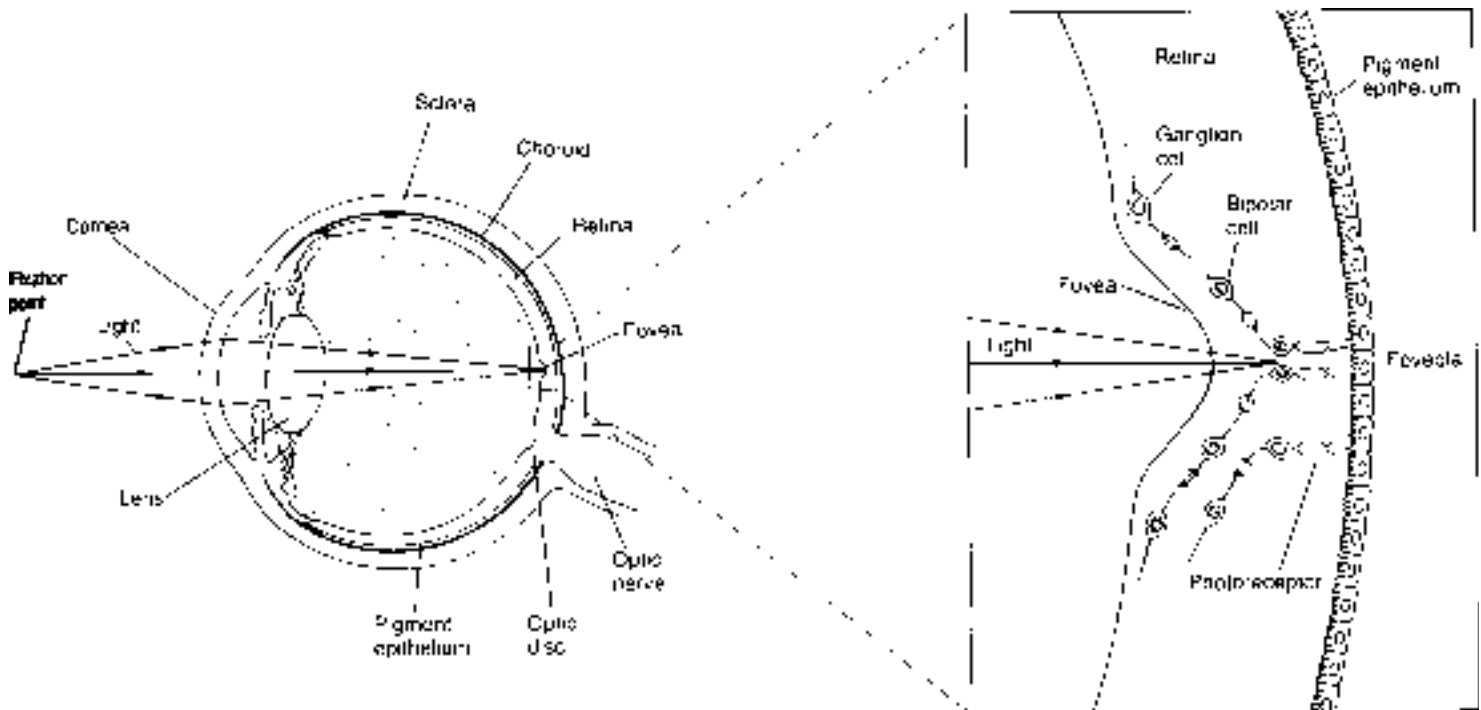
This section discusses the retina, where light energy is converted into neural signals and the neural processing of vision begins.

A. BASIC RETINAL ANATOMY

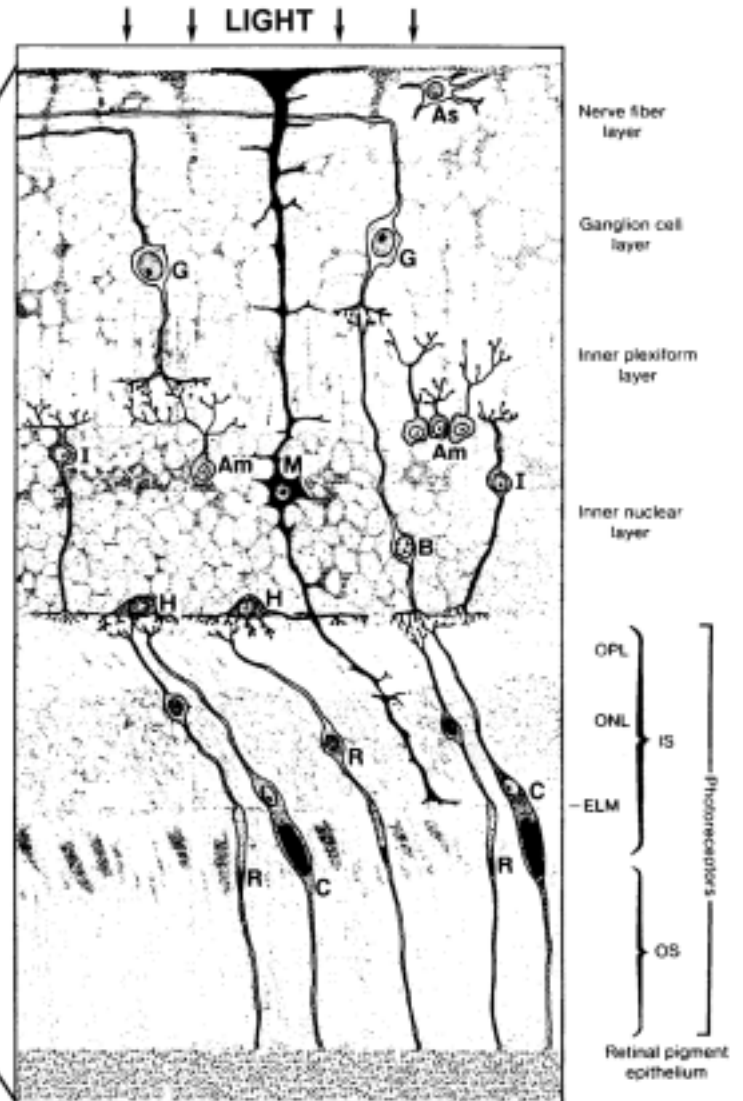
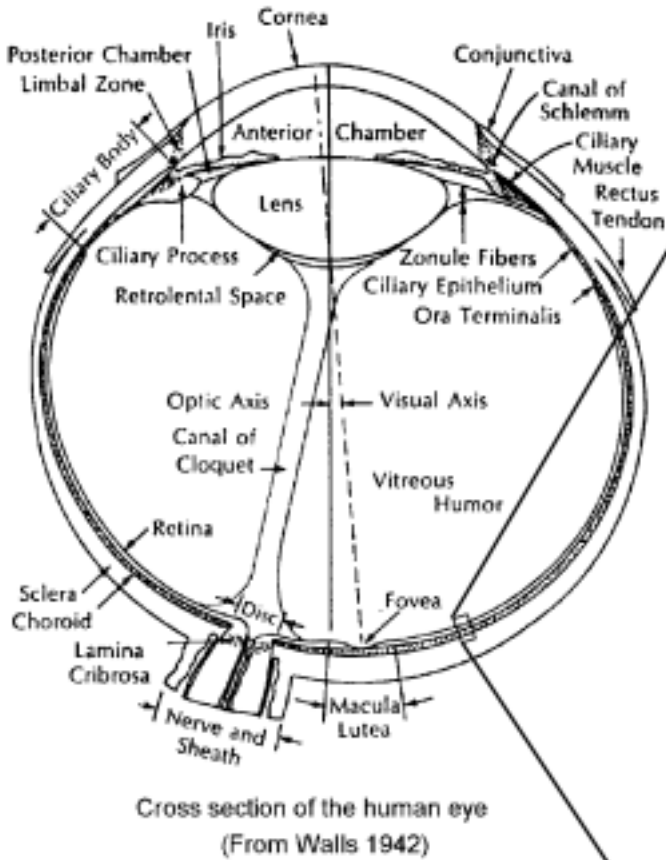
The retina thinly covers the posterior half of the eye and is a highly layered structure when viewed in cross section. The layers alternate between those that contain *cell bodies* of retinal cell types (the **nuclear layers**) and those that contain a web-like plexus of *axonal and dendritic processes* where different cell types interact (the **plexiform layers**).

The layers of the retina are named according to their cellular makeup and for their position in the retina. Cell bodies reside in cell or nuclear layers. Synapses form in plexiform layers. Thus, starting in the outer (towards the sclera) portion of the retina, adjacent to the pigment epithelium and continuing inward toward the vitreous, there is the:

- photoreceptor layer (contains the light-transducing cells of the eye)
- external limiting membrane
- outer nuclear layer (contains the nuclei of photoreceptors)
- outer plexiform layer
- inner nuclear layer (contains bipolar cells and other integrative neurons of the retina)
- inner plexiform layer
- ganglion cell layer (contains ganglion cells!)
- nerve fiber layer (ganglion cell axons, headed to the optic disc to form the optic nerve)



Cross section through the human eye (from Kandel et al 1991). Rays of light enter anteriorly, pass through the optical structures and end up on the back of the eye at the retina. Detail of the retina at the fovea is shown on the right



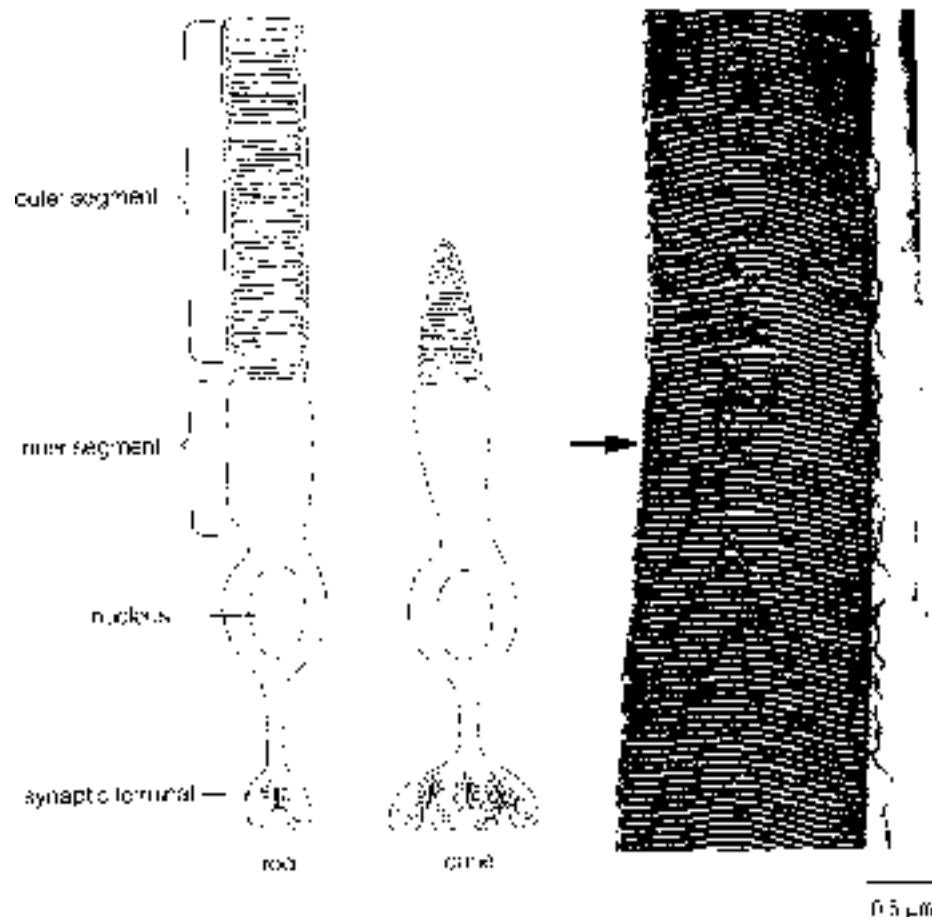
Schematic drawing showing layers and circuitry of the adult retina (from Miller, 1982). OPL, outer plexiform layer; ONL, outer nuclear layer; ELM, external limiting membrane; OS, outer segments of photoreceptors; IS, inner segments of photoreceptors; Am, amacrine cell; As, astrocyte; B, bipolar cell; C, cone photoreceptor; G, ganglion cell; H, horizontal cell; I, interplexiform cell; M, Muller cell; R, rod photoreceptor

Notice that the horizontal cross section of the eye on the left is in the same orientation as the schematic figure on the right that labels the layers of the retina. This means the rays of light are coming in from the top of the page and the photoreceptors, the light sensitive elements in the retina labeled “R” and “C”, are at the bottom of the figure. This retinal picture highlights the main cell types and their connections with one another, but does not convey how highly packed the retina is with cells. So, light must pass through neural, glial and vascular elements before it finally reaches the light-sensitive photoreceptors in the outer nuclear layer. This means that you have an **inverted retina!** It’s inverted because the neural layers of the retina overlie the photoreceptor layer, and actually come between the light source and the photoreceptors.

Obviously, this organization must degrade the visual image that reaches the photoreceptors, so much of the retina is specialized to become as transparent as possible. First, the axons in the retina are unmyelinated (myelin is fairly opaque). Further, the retina itself is very thin (about 0.4 mm thick), with few structural supporting elements, and the walls of the blood vessels that supply the retina are thin as well. The price for this transparency is a fragile retina. So the retina must balance the need for optical transparency with its high metabolic needs. With so little support the retina is susceptible to tearing away from the choroid. Dr. Heatley will discuss retinal detachment in a later lecture.

The structure of the retina is qualitatively similar along its entire extent, except for two important places. One is the **optic disc**, which is the place where the axons of retinal ganglion cells depart the eye and blood vessels access the eye. The second place is the **fovea**, which is a pit-shaped area in the central retina (about 1.5 mm wide) where the retina is reduced to half its normal thickness. The fovea is specialized for best visual acuity (more on this later), and it subserves visual fixation (the ability to look directly at a visual target with your best vision). When you are look directly at an object, light from that object falls upon the fovea.

The fovea is at the center of a slightly larger region (about 6 mm in diameter) called the **macula lutea**, (or simply, the macula). When you look into the back of the eye in clinic, the macula will have a yellowish appearance compared to the rest of the retina, and you know that the fovea is located in the center of this area. Because of this overlap, the terms “foveal vision” and “macular vision” are often used interchangeably. (The yellowish appearance of the macular region of the retina is due to a yellow pigment that absorbs blue/violet light to protect retinal cells from light damage.)



The two photoreceptor types in the retina.

B. CELL TYPES IN THE RETINA

Photoreceptors

Photoreceptors are those unique cells in the retina that transduce light energy into a neural signal. There are two types of photoreceptors, **rods** and **cones**. Cones have a cone-shaped 'head' to them and rods are shaped like— a rod!! Both rods and cones have traditional cellular machinery in their cell body, but possess a distinct functional region in the distal portion of the cell called the **outer segment**. The outer segment is densely packed with light-sensitive molecules in a series of invaginations in the cell membrane that resembles a stack of discs. When photons of light impact on the photosensitive material in the outer segment, they initiate a cascade of biochemical events within the photoreceptor that signals the presence of light. Rods and cones do not fire action potentials, but instead respond with *graded changes in membrane potential*.

A photoreceptor forms a synaptic contact with a bipolar cell (and other neural cells). The region of synaptic contact is the outer plexiform layer (OPL) of the retina. In turn, the bipolar cell synaptically contacts a ganglion cells in the inner plexiform layer (IPL) of the retina. The ganglion cell then sends its axon across the inner (inner = vitreal) surface of the retina, along with many other ganglion cell axons. (This is called the nerve fiber layer in your retinal diagram.) The ganglion cell axons head towards the optic disc, where the axons depart the eye.

Therefore, the most direct neural path out of the eye is the following:

- 1) **Photoreceptors**, the light-sensitive cells, contact
- 2) **Bipolar cells**, which are neurons that synapse on
- 3) **Ganglion cells**, which send their axons to the brain.

After two synapses, you're out of the retina and into the brain.

Other retinal cell types

Retinal circuitry is actually more complicated, not surprisingly. Other neurons in the retina can form local neural circuits within the retina. Photoreceptors can contact not only bipolar cells, but also **horizontal cells** that sit in the outer nuclear layer. One horizontal cell can contact numerous photoreceptors. **Interplexiform cells** and **amacrine cells** in the inner nuclear layer form neural circuits with bipolar cells and ganglion cells. The neural connections formed by these cells ensures that neural messages flow laterally within the retinal layers, as well as across the layers. The neural processing of visual signals doesn't start in the brain; it starts in the retina.

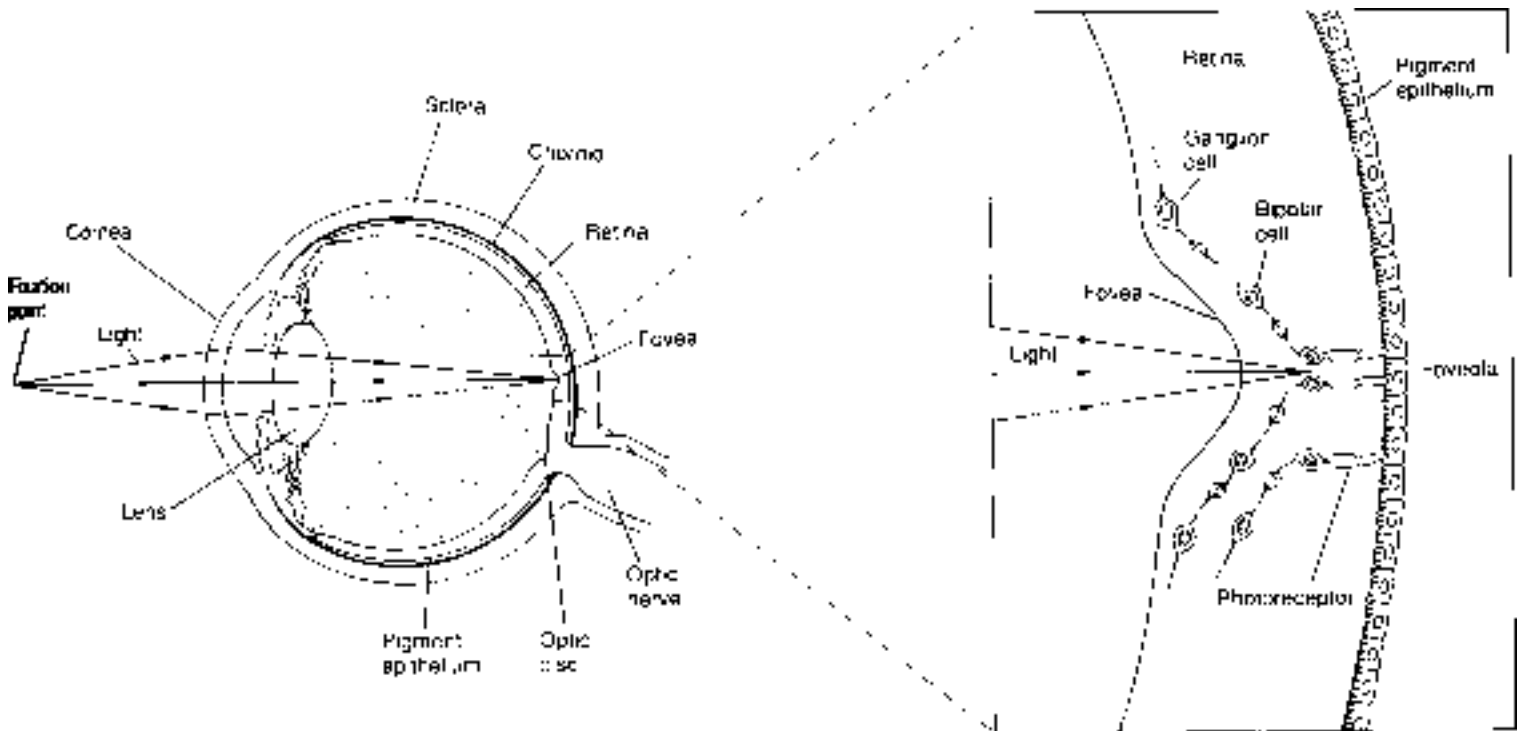
There are also non-neural cell in the retina, retinal astrocytes and large glial cells (**Muller cells**) that provide metabolic support for the retina, but they will not be discussed further.

You are not expected to memorize the entirety of retinal circuitry. Just know that these additional retinal circuits begin the neural crafting and analysis of the visual image, making the visual receptive fields of retinal ganglion cells more sophisticated than those of the photoreceptors.

C. RETINAL PIGMENT EPITHELIUM

The tips of the photoreceptor outer segments contact (“stick their heads into”) the **retinal pigment epithelium (RPE)**. The retinal pigment epithelium is a layer of melanin-containing cells on the internal side of the choroid. Although pigment epithelial cells are not neurons, they are important for retinal function:

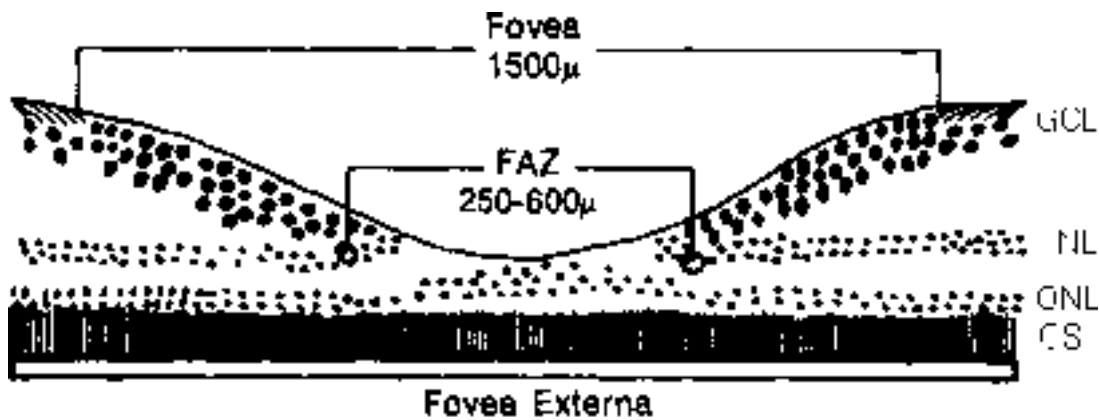
- The RPE contains **melanin**, a black pigment that absorbs light not captured by the photoreceptors. This absorption prevents the reflection and scatter of light that would degrade the visual image, and it helps to cool the photoreceptors from the heat of the absorbed light.



Cross section through the human eye (from Kandel et al (1991)) Rays of light enter anteriorly pass through the optical structures and end up on the back of the eye at the retina Detail of the retina at the fovea is shown on the right

- The retinal pigment epithelium is important metabolically. It is involved in the regeneration of the light-exposed photosensitive material within photoreceptors and is a disposal/recycling system for old photoreceptor outer segment discs. Photoreceptor discs in the outer segment are constantly undergoing turnover. Older discs are shed (about 3/hr) from the top of the outer segment while new discs are generated where the outer segment connects to the rest of the cell body. This turnover of discs depends critically on the retinal pigment epithelium.

Retinal pigment epithelial cells may weaken with age and then function less efficiently. Problems with retinal pigment epithelial cell function can have devastating effects on the dependent photoreceptors and lead to progressive blindness. This is especially true in the macular region of the retina because the numbers of photoreceptors are extremely high, putting a greater load on the retinal pigment epithelium there. Dr. Heatley will discuss age-related macular degeneration later in the module.



Cross section through a human fovea. FAZ - Foveal avascular zone

D. SPECIALIZATIONS IN THE RETINA

THE FOVEA

When you are looking carefully at, fixating, an object, the image of that object is focused on the region of the retina called the fovea. The **fovea** mediates your most acute vision with special characteristics.

The fovea looks anatomically like a pit, or depression in the retina. The pit forms in the vitreal side of the retina because the retina here contains only the photoreceptor layer. The other types of retinal neurons and the blood vessels are displaced to the edge of the fovea. The dots in the schematic diagram of the foveal region represent retinal cell bodies. The layer of largest dots is missing from the central fovea because the ganglion cells (GCL) are pushed to the side there. The cells in the inner nuclear layer (INL) are also pushed to the side. The only dots found in the central fovea are those of the outer nuclear layer (ONL), which are the cell bodies of the photoreceptors, and they are especially densely packed together. So, the foveal pit removes interference from other layers of retinal cells and enables light to reach the cone photoreceptors in the most direct manner possible.

In addition, the fovea contains the highest density of cone photoreceptors anywhere in the retina, and cones mediate high visual acuity and color vision. This cone-packed region ensures that central vision is as acute as possible. You will see that the high neural commitment to central, macular/foveal vision is continued in the visual thalamus and cortex.

ROD- AND CONE-MEDIATED VISION

Photoreceptors come in two kinds, rods and cones. However, photoreceptor cones differ from rods in more ways than just the shape of their outer segments, and this has important significance for human vision.

Cones underlie our daylight vision, our color vision, and our central vision (or best acuity vision).

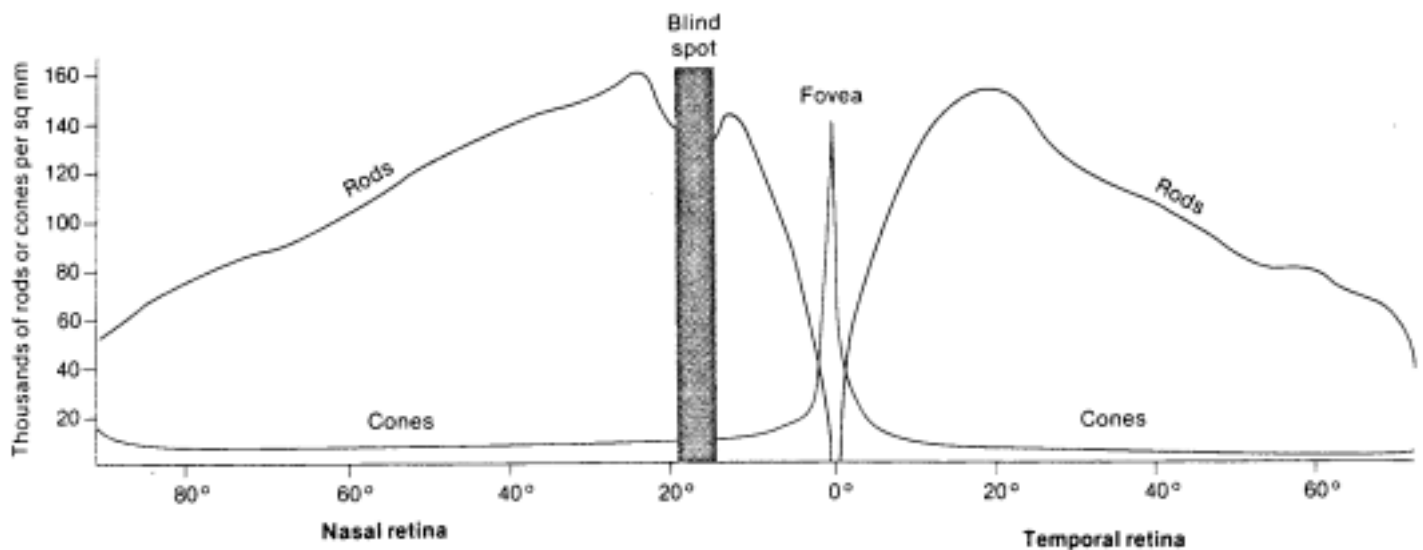
Rods underlie our night vision, our highest sensitivity vision, and our peripheral vision.

Several differences in the rod and cone systems lead to their different functions:

- *Rods and cones are distributed differently across the retina:*

Cones are greatest in number in the fovea. In fact, they are the only type of photoreceptor found in the fovea and are densely packed. The number of cones drops substantially by 15 degrees away from the fovea on both the nasal and temporal sides of the retina and throughout the peripheral retina, although cones do not disappear entirely.

Rods are absent from the fovea. Nevertheless, rods are the primary receptor in non-foveal regions of the retina, which comprise the majority of the retina. Rods peak in numbers in the perifovea, and become less numerous, but still are dominant in more peripheral regions of the retina.

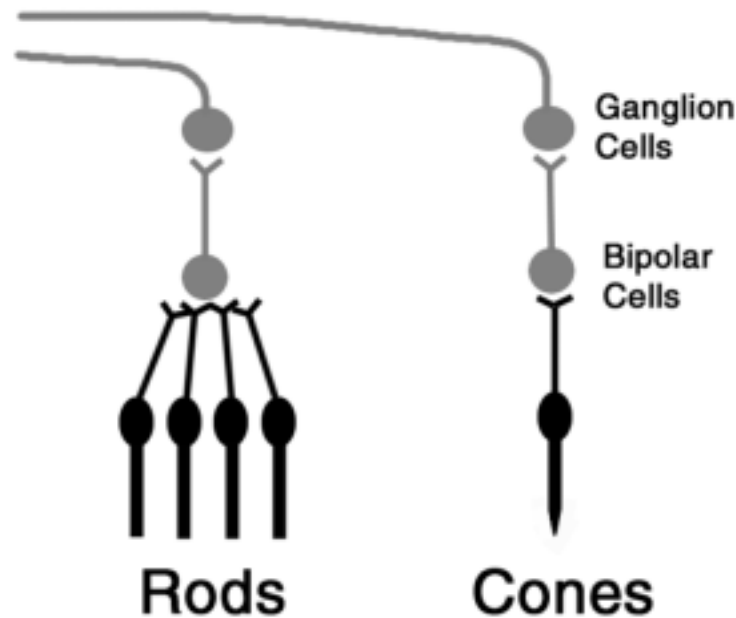


Distribution of rods and cones across the retina. Note the region called the **Blind Spot** in the nasal retina where there are no photoreceptors. This corresponds to the optic disc (or optic nerve head).

- **Rods are more sensitive to light than are cones:**

Rods are highly sensitive in dim lighting conditions, and they underlie night vision. Light that is too weak to stimulate cones may still activate rods. In fact, a single photon of light can stimulate the most sensitive rods.

Convergence in the Rod System



Under dim or **scotopic** (G. *skotos*, darkness) lighting conditions, the position of greatest acuity on the retina is not in the fovea, but rather the perifovea, where the density of rods is highest. You can demonstrate this to yourself by getting dark adapted (by sitting in the dark for 20 minutes) and looking at the stars at night (avoiding the bright lights of the big city!). If you try to fixate a very dim star, it will disappear, but it can reappear if you move your point of fixation to one side (moving the image of the star off the fovea and on to the region of maximal rod density).

Rods are famous for pooling their contributions so that one bipolar cell gets input from many rods. This is called **convergence**. The convergence in the rod system is great for increasing sensitivity to weak visual stimulation, but isn't optimal for fine analysis.

Not surprisingly, a number of nocturnal animal animals have all-rod retinas. When the rods fail in humans, leaving only cones, people can see reasonably well during the day, but they suffer from "night blindness" in dim light and at night.

- **Cones have better acuity than rods.**

Cones require good lighting conditions and mediate our excellent daytime, photopic (G. *phot*, light) vision. Cones require more light than do rods, but once stimulated, cones underlie some of the most important characteristics of our visual system: excellent daytime vision, high visual acuity, and color vision. A number of features contribute to higher acuity. First, cones are very densely packed in the fovea.

Furthermore, foveal cones can have one-to-one connections with bipolar cells and connections where relatively few cones provide input to a bipolar cell. The more individualized cone-to-bipolar-to-ganglion cell connections allow the cone system to better resolve and convey fine details of retinal illumination (= acuity) that the rod system just cannot.

People who lose their central, macular vision and cone function are left with rod-mediated vision and are legally blind (20/200 vision; more on this disease and vision terminology later).

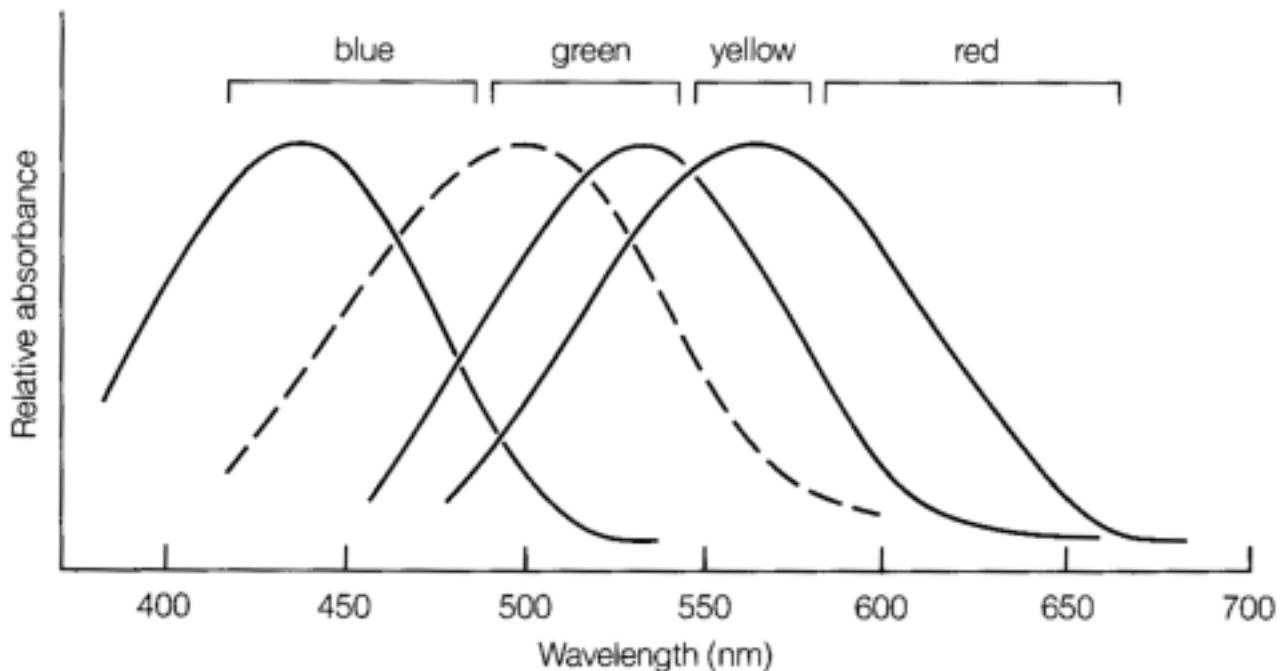
- ***Rods are much more common than are cones:***

120 million rods, 6 million cones. In addition, there are only 1 million ganglion cells. Thus, there is considerable convergence of photoreceptors onto ganglion cells, and there is *more convergence in the rod system than in the cone system*.

- ***Cones convey color information; rods don't:***

All rods contain one light sensitive photopigment, **rhodopsin**. Rods “see” the world in shades of black and white, signaling only the presence or absence of light. This is why the world looks gray and colorless when you awaken in very dim light in the middle of the night and must rely on your rod vision to see.

Cones contain one of *three* different photopigments. Like the rhodopsin in rods, the photopigment in cones is composed of two parts: retinal and a cone opsin. The spectral response of cones differs depending on which of the three cone opsins is contained in the given cell. (Remember, each cone contains only one photopigment).



The relative absorption spectra (comparison of how much light is absorbed) of the four visual pigments in the eye across the visible spectrum of light. The three cone pigments are shown in solid lines and the rod pigment, **rhodopsin**, is denoted by a dashed line. Most visible light is absorbed by more than one type of photoreceptor. For example, a pure yellow light, around 575nm, would be well absorbed by one type of cone pigment (from longwave sensitive cones), moderately well absorbed by the middlewave sensitive cone pigment, and poorly absorbed by rod pigment.

Cones are referred to as shortwave sensitive, middlewave sensitive, and longwave sensitive types because they absorb light maximally in three different regions of the visible spectrum of light. This terminology is commonly simplified to ‘*blue cones, green cones, and red cones*’, respectively. It is the combined contribution of the three cone types that leads to our ability to perceive and discriminate a full range of color.

People who exhibit a color deficiency, or are “color blind”, are most often male (x-linked genetics is involved) and either have an anomalous pigment in one type of cone or are actually missing one of the cone types. Such individuals still see the world in color, but in somewhat different hues or in fewer hues than people with typical color vision.

Comparison of Rod- And Cone-Mediated Vision

Rods

Many rods (120 million)
Night (scotopic) vision
Very sensitive to light
Work in dim light
Convergent neural paths
Low visual acuity (20/200)
Black & white vision
Best in periphery

Cones

Few cones (6 million)
Day (photopic) vision
Less sensitive to light
Work in bright light
More direct neural paths
High visual acuity (20/20)
Color vision (trichromatic)
Best in fovea

Peripheral versus Central Vision

It’s useful to think about retinal function by comparing rod- and cone-mediated vision, but it is also helpful to think in terms of peripheral versus central vision. This is useful not only because the retina doesn’t totally segregate rods and cones, but because the peripheral retina and the central retina (i.e. the macular/foveal region) are designed to have different jobs in everyday vision.

The peripheral retina is quite good at noticing things, particularly objects moving in the periphery of your field of vision. You can consider the *peripheral retina* to be an *image locator*. It detects new stimuli. Your oculomotor system does a superb job of quickly calculating exactly what muscle movement is required to rotate the eye to bring the image of that interesting object from the peripheral retina to the fovea.

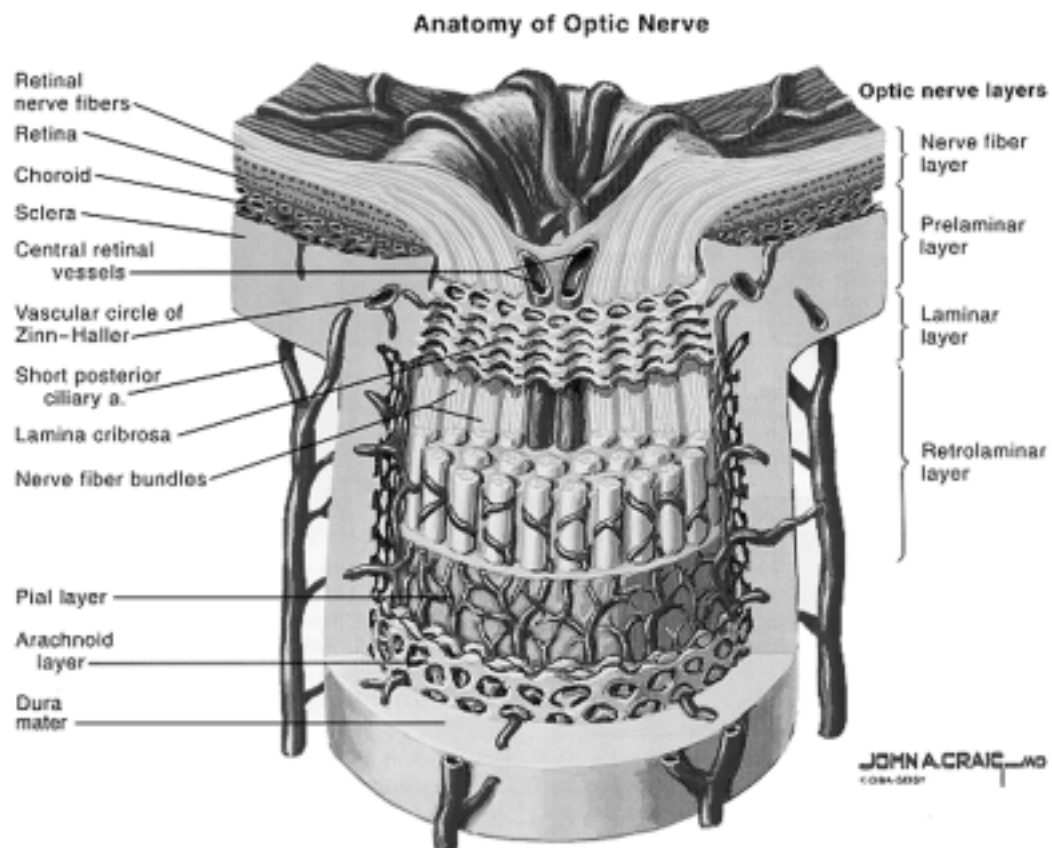
The peripheral retina isn’t very good at telling what that object is. That’s the job of the central retina. Once your oculomotor system fixates an object, the image of that object falls on your fovea. The *central retina* then acts as an *image analyzer*, enabling you to examine and process the object in detail.

E. OPTIC DISC AND OPTIC NERVE

Once the job of the retina is completed, the axons from a million retinal ganglion cells traverse the surface of the retina to the nasal retina and exit the eye at the **optic disc**, also called the **optic nerve head**, becoming the **optic nerve** as they head posteriorly as a bundle towards the brain. The optic nerve is covered in a dural sheath. That is contiguous with the dura mater of the cranium.

The pressure and fluids within the eye are different from that in the rest of the brain, so there is a barrier at the base of the optic nerve made of specialized sclera called the **lamina cribrosa**. The lamina cribrosa is made of dense collagen with fenestrations through which the axons and neuroglia pass. The lamina cribrosa contains some elastin to adapt to variations in intraocular pressure.

The ganglion cell axons first become **myelinated** in the optic nerve. Starting at the region of the lamina cribrosa, the axons are enwrapped by oligodendroglial cells and grouped into small bundles by astrocytes and microglia. The individual nerve fibers in the optic nerve display a modest degree of organization that reflects the site of origin of a ganglion cell on the retina. So, most axons that come from a particular quadrant of the retina tend to be grouped in the same region in the nerve:



Schematic diagram of the optic disc. Note that the tough, outer portion of the sclera of the eye joins with the dura of the optic nerve. This forms a continuous protective sheath for the ganglion cell axons that are bundled together to form the optic nerve.

Axons derived from central retinal locations tend to occupy central locations in the optic nerve. Axons coming from the peripheral retina lie in peripheral portions of the nerve.

Thus, when a disease process damages a small portion of the optic nerve, the corresponding portion of the retina, but not the entire retina, is affected.

The optic disc and nerve can present their own clinical concerns. The optic disc provides the interface between the eye and the cranium. Therefore, infections within the eye (endophthalmitis) can follow the same route as the ganglion cell axons from the eye to the brain to become meningitis or encephalitis. Sensory nerves are contained in the dural sheath of the optic nerve. This partly explains the pain that some patients experience with optic nerve diseases, such as optic neuritis.

Blind spot associated with the optic disc. Normally you don't notice the blind spot in your field of vision because it is 'filled in' perceptually by the brain. However, you can demonstrate the blind spot to yourself by closing one eye and fixating the "X" in the adjacent figure. Now slowly move the page to about 30 cm away. At a certain distance, one set of the words "BLIND SPOT" should disappear, but not the other set. Now repeat the test with the other eye. Which side of the visual field (nasal, toward the nose, or temporal, toward the temple) has the blind spot this time? Notice that the vertical lines do not appear to have a clear hole in them.



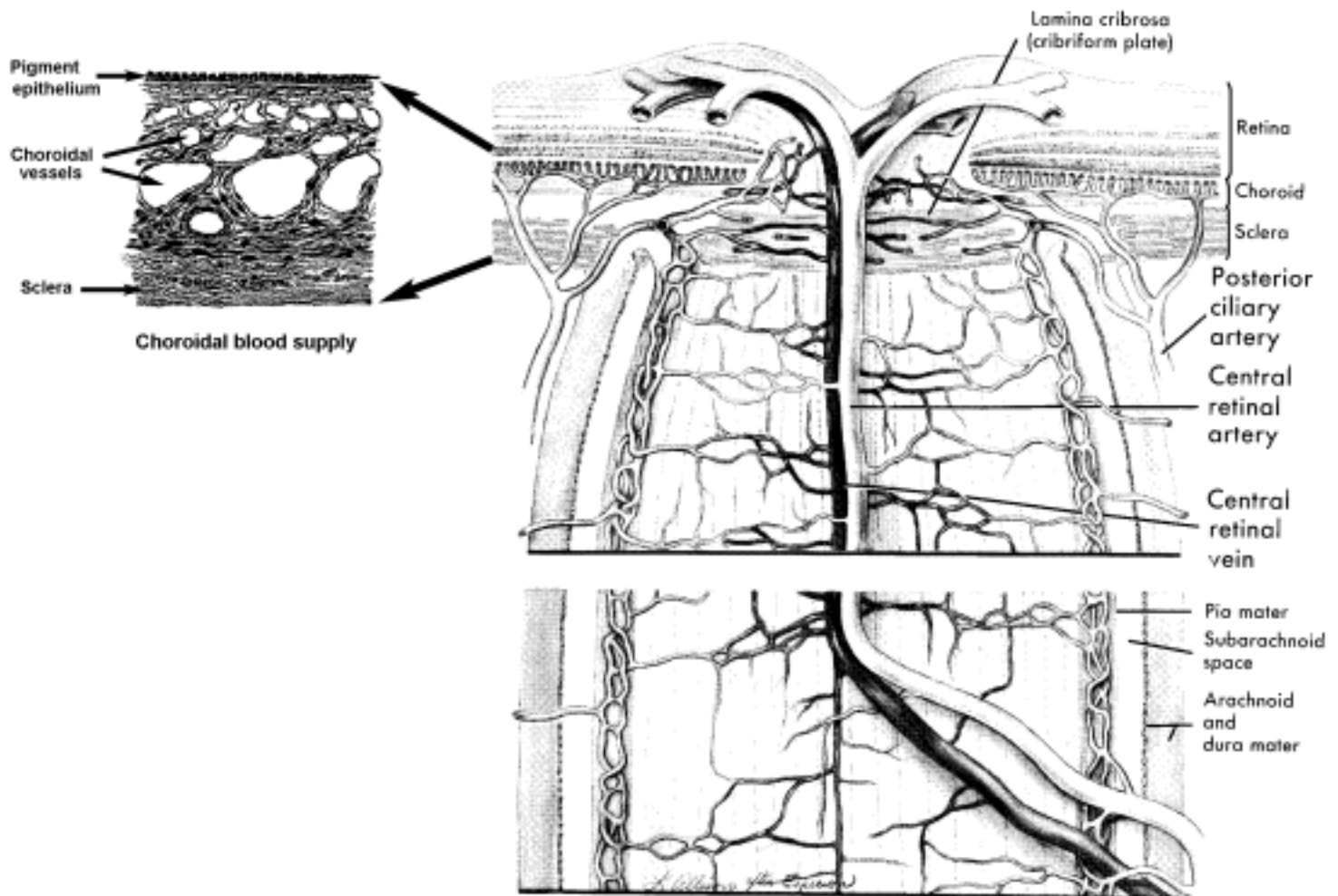
Demonstration of the blind spot caused by the optic disc.

A pathological blind spot is called a scotoma and may be caused by a lesion in the eye or in part of the visual pathways. After this demonstration you can see why patients can have scotomas and not be aware of them.

F. BLOOD SUPPLY

Retina

The retinal blood supply comes from two sources. The **central retinal artery**, a branch of the **ophthalmic artery**, enters the eye through the **optic disc**. The central retinal artery branches out over the retinal surface to supply the **inner 2/3 of the retina** (i.e., towards the vitreous). Occlusion of the central retinal artery results in sudden and usually irreversible loss of vision.



A dense network of **capillaries in the choroid layer** (the **choriocapillaris**) supplies the remaining **outer retina**, most notably the **photoreceptors**, via regulated transport across the retinal pigment epithelium. The choroidal vasculature is supplied by the **posterior ciliary artery**, a branch of the **ophthalmic artery**.

Optic nerve

The **optic nerve** is supplied by the **central retinal artery** and by the **posterior ciliary arteries**, which travel *outside* of the optic nerve, external to the dural sheath.

Practice Questions

Practice Questions — Retinal Structure and Function

1. Match each retinal structure in the left column with the most closely associated item in the right column:

- | | |
|------------------------|---|
| ganglion cell axons | A. glial cells |
| horizontal cells | B. found in the innermost cell body layer of the retina |
| photoreceptors | C. the tips of the photoreceptors are embedded in this |
| ganglion cell bodies | D. located in the outermost layers of the retina |
| Muller's cells | E. photoreceptor-less area where ganglion cell axons exit the eye |
| bipolar cells | F. provide for many lateral interactions in the retina |
| retinal pigment epith. | G. connect photoreceptors to ganglion cells |
| optic disc | H. the neural output of the retina |

2. True or False:

- A. the choroid contains no blood vessels
- B. the jobs of the retinal pigment epithelium include metabolizing used photoreceptor outer segments and absorbing stray light
- C. horizontal and amacrine cells primarily make lateral connections within the retina while bipolar cells primarily make connections between photoreceptors and retinal ganglion cells
- D. nerve fibers corresponding to the macula are located in the center of the optic nerve
- E. the lamina cribrosa is a membrane that separates layers of the retina

3. The reason that ganglion cell axons are not myelinated within the eye is:

- A. to increase speed of signal transmission
- B. to enable summation of neural signals
- C. to allow a graded response to light
- D. to make the retina more transparent to incoming light
- E. to make life just a bit more complicated for first year medical students

4. Match each characteristic to either RODS or CONES:

- A. function best in dim light
- B. predominate in the fovea
- C. complete loss results in night blindness
- D. relatively low photoreceptor-to-ganglion cell convergence ratio
- E. may be stimulated by a single photon of light
- F. mediate scotopic vision
- G. function best in bright light
- H. complete loss results in poor visual acuity
- I. mediate photopic vision
- J. mediate color vision
- K. the most common type of photoreceptor in the retina

5. The **FOVEA** is associated with which of the following characteristics (more than one answer is correct):
- A. rods
 - B. heavily supplied by surface blood vessels
 - C. high acuity vision
 - D. a pit in the retinal cell layers
 - E. central vision
 - F. Schlemm's canal
 - G. alerting you to a projectile hurtling toward you from the left
6. Name the site of acquisition of myelin by axons in the visual path:
- A. ganglion cell body
 - B. bipolar cell axons
 - C. macula lutea
 - D. lamina cribrosa
 - E. fovea
 - F. optic nerve as it leaves the orbit
7. A patient has lost all the rods in her retina. Which of the following statements regarding her condition is **TRUE**?
- A. she can no longer discriminate different colors
 - B. her visual acuity is now best in the parafovea
 - C. she has lost most of the photoreceptors in her retina
 - D. her visual acuity at night is unaffected, but her photopic acuity is devastated
 - E. all of the statements are true
8. Which of the following statements is **TRUE**?
- A. the retina is inverted such that light coming into the eye must pass through the other cell types before it reaches the photoreceptors
 - B. the optic disc is located in the temporal retina (the part nearest your temple)
 - C. the optic disc is specialized for best visual acuity
 - D. the foveal pit in the nasal retina (the part nearest your nose) is where the ganglion cell axons depart the eye to form the optic nerve
 - E. the foveal pit is the retinal mosh pit, where photoreceptors slam into each other and crowd surf while listening to punk rock
9. Let's try another one on rods and cones. Which of the following statements is **FALSE**?
- A. there are more rods than cones in the retina.
 - B. cones are most numerous at the fovea, while rods are most numerous at the optic disc
 - C. cones mediate color vision, while the rod system is achromatic
 - D. individual rod photoreceptors are more sensitive to light than are cone photoreceptors; this is one reason that the rod system functions well under scotopic conditions
 - E. the cone system exhibits better visual acuity in part because there is less synaptic convergence in the cone system

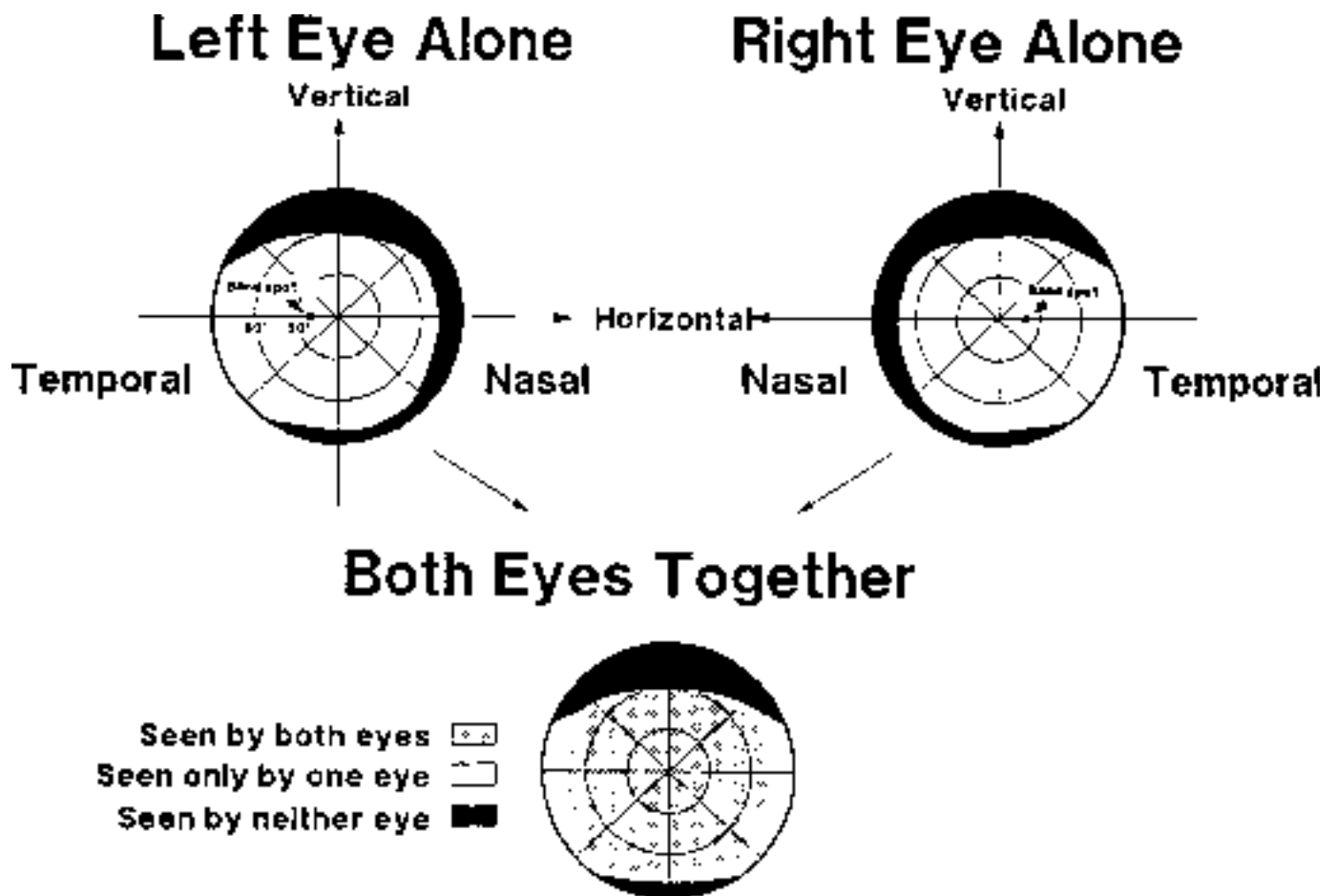
RETINAL STRUCTURE AND FUNCTION: PRACTICE QUESTION ANSWERS

1. ganglion cell axons - H
horizontal cells - F
photoreceptors - D
ganglion cell bodies - B
Muller's cells - A
bipolar cells - G
retinal pigment epithelium - C
optic disc - E
2. A - F
B - T
C - T
D - T
E - F
3. D; and E (but just a little bit)
4. A - rods
B - cones
C - rods
D - cones
E - rods
F - rods
G - cones
H - cones
I - cones
J - cones
K - rods
5. C, D, E
6. D
7. C
8. A
9. B (there are no photoreceptors at the optic disc)

CENTRAL VISUAL PATHWAYS

Next we examine the central visual pathways, through the optic nerve to cortical structures, and see how these pathways map the visible world.

Visual areas in the brain commonly contain an organized ‘map’ of the visual world. Understanding this visual mapping, “visuotopy”, is important for understanding the central projections of visual neurons and the deficits that accompany damage to central visual structures. We start by defining terms relating to the field of vision and visual topography.



A. Visual Fields And Retinal Coordinates

The **visual field** of an eye is the entire extent of the external world that can be seen without moving the eye. Locations in the visual hemi-field (half-visual field) of an eye closer to the person's nose are referred to as the **nasal field**. Locations in the visual hemi-field closer to the temple are in the **temporal field**. The visual field can also be divided into an upper half or **superior field** and a lower half or **inferior field**. The combination of the two monocular fields is the **binocular field**.

MONOCULAR AND BINOCULAR VISUAL FIELDS.

The two upper charts in the visual field figure are for the left and right eye *individually*, so they are called **monocular fields**. The center of each corresponds to the point of central fixation (the fovea). White areas indicate visual field locations that can be *seen* by that eye. Black areas cannot be seen. The receptor-less blind spot (the optic nerve head) is also shown.

The bottom chart is obtained by superimposing the two monocular visual fields. Parts of the field that are seen by both eyes are shaded; this is the **binocular field**. The white areas in the far temporal fields of both sides are seen only by one eye or the other. They are known as the **monocular segments** or monocular crescents.

Two coordinate systems are used for localizing a visual deficit:

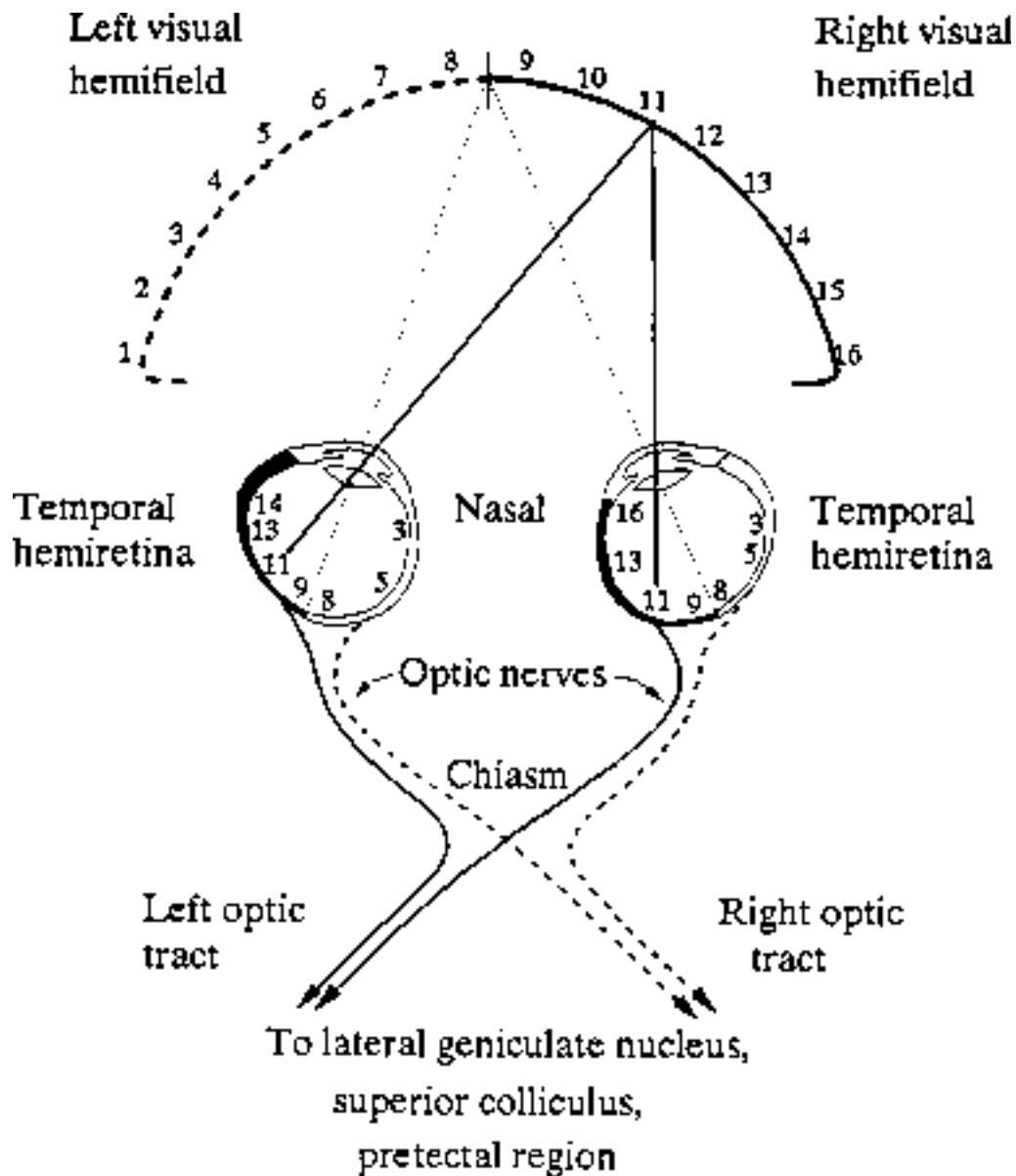
- 1) **visual field coordinates**, just introduced, which refer to locations *in the field of vision*
- 2) **retinal coordinates**, which refer to the corresponding location of the visual image *on the retina*
Retinal coordinates describe locations in anatomical terms. For example, we can refer to the nasal or temporal half of a retina, or to the superior or inferior retina.

Locations in the visual field correspond to specific locations on the retina. Both retinal and visual field coordinate systems are used. It is important that you understand which coordinate system is in use when describing the location of a visual deficit. Otherwise, the terms “nasal” and “temporal,” “superior” and “inferior”, and even “ipsilateral” and “contralateral,” are meaningless.

Important point: The image is inverted as it passes through the lens. Thus, light from the nasal visual field projects to corresponding locations on the temporal half of the retina and vice versa. Similarly, light from the superior visual field falls on the inferior retina and vice versa.

Normally, the two retinae are in register such that a visual image falls on corresponding points on the two retinas, and the object is seen as a single image. However, if one eye deviates (remember Dr. Harting’s brainstem lesions?), then double vision or **diplopia** results. You can demonstrate this by fixating an object and then changing the alignment of the one eye by very gently pressing on one side.

A final point on topographical organization in the visual pathways: This organization begins in the retina, where adjacent cells in the retina “look” at adjacent points in the field of vision. The region in the visual field that a neuron “sees”, or more accurately, the region in visual space in which a visual stimulus can excite or inhibit a visual neuron is called the **visual receptive field** of the cell. Think of the entire visual field as the sum of all the little receptive fields of your visual neurons. The topographic organization in the visual system is referred to as **retinotopic organization**. As you will see, retinotopy is maintained in the central visual pathways.



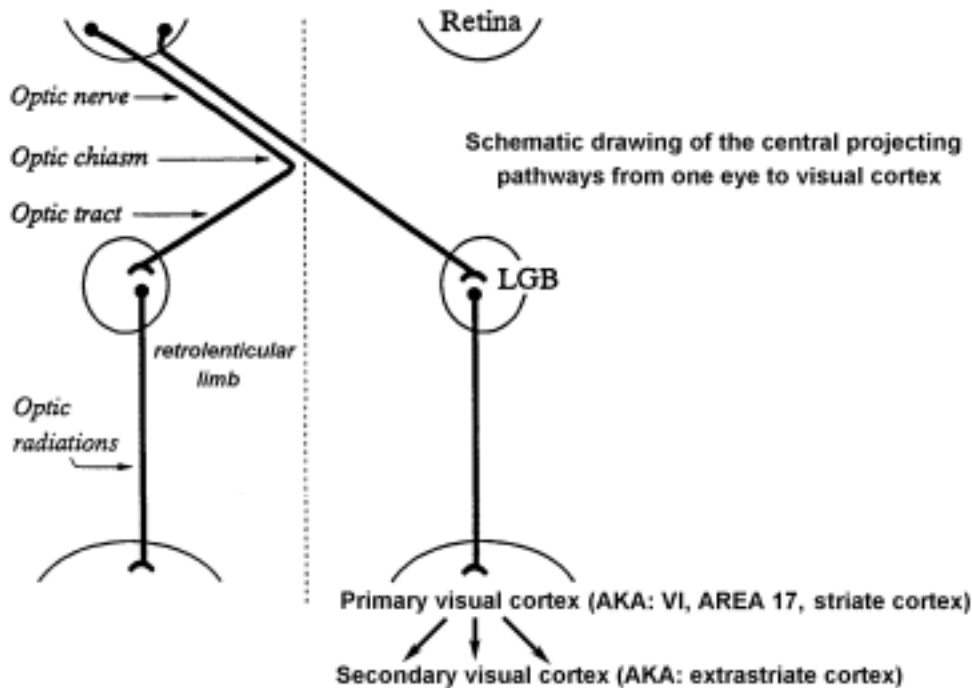
Retinotopic organization in the ascending visual pathways. The numbers represent different points along the horizontal meridian and their projections onto the retinas of the two eyes. Optic tract axons headed *toward the left* side of the brain are shown in *solid* lines; those bound *for the right* side are *dotted*. Note that each side of the brain gets input from points in the *contralateral* visual hemifield.

B. Retinal Projections

Retinal ganglion cells provide the sole neural output of the retina, and they project a long way. After exiting the optic disc, the axons of ganglion cells traverse in the optic nerve to the **optic chiasm** (G. *chiasma*, two crossing lines) where decussation occurs. Once the axons have passed the optic chiasm, they are renamed the **optic tract**.

At the optic chiasm, many of the axons cross over to join the contralateral optic tract, but some axons remain uncrossed and continue along on the ipsilateral side. So, unlike the optic nerve, the optic tract contains axons from *both* eyes. There is a simple order to the crossing. Axons from the nasal retina cross to the contralateral optic tract, while those from the temporal retina remain in

the ipsilateral optic tract. As a result, central visual structures receive afferent visual input from the eyes that represents one-half of the visual field, the *contralateral visual field*.



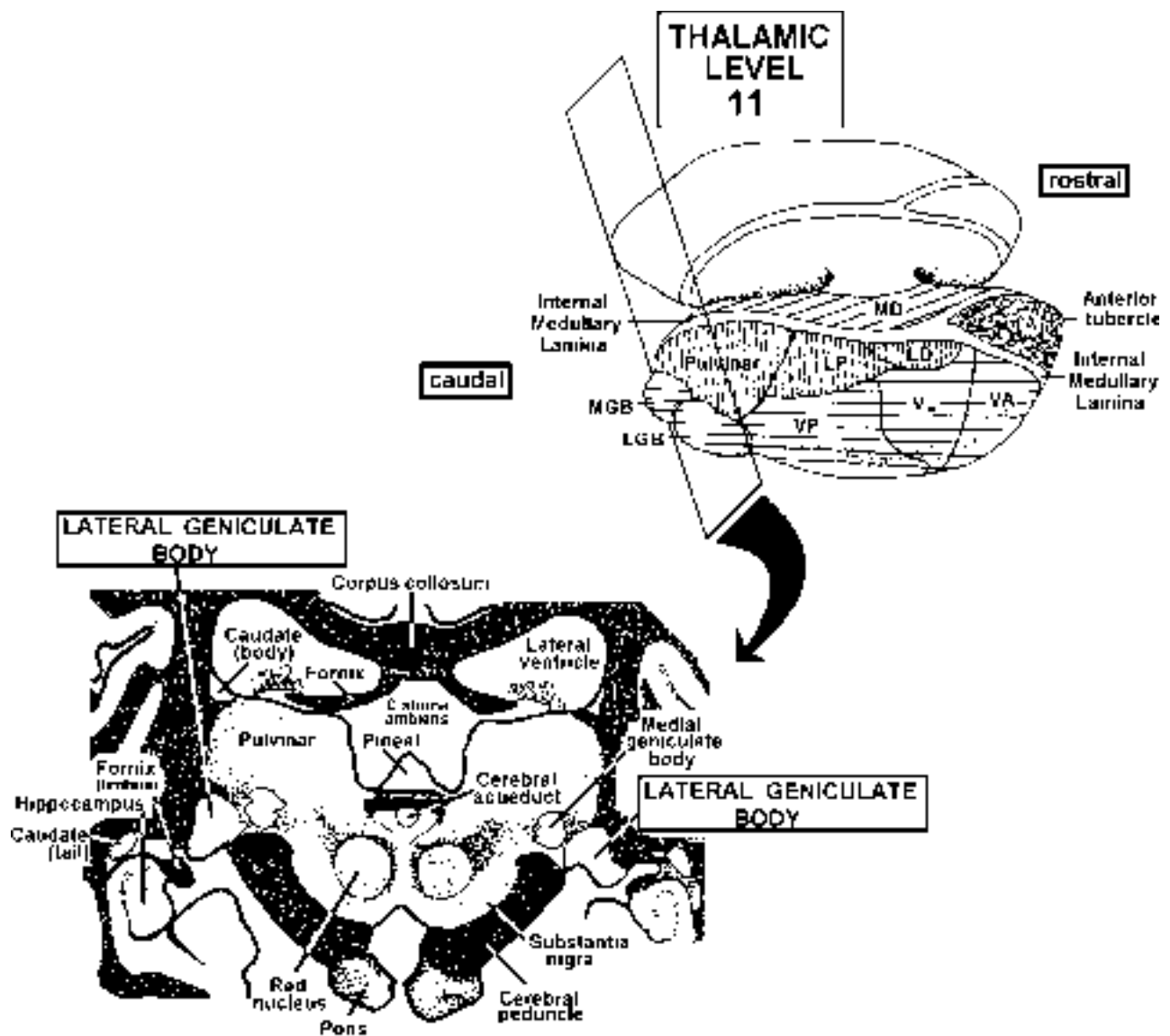
OVERVIEW: Retinal ganglion cell axons project to a number of locations in the brain, primarily to:

- **thalamus** (lateral geniculate body), pathway for conscious visual perception.
- **superior colliculus**, involved in saccadic eye movements and orienting responses.
- **pretectum**, involved in pupillary light reflex and a primitive eye movement reflex called optokinetic nystagmus.
- **hypothalamus** (the suprachiasmatic nucleus), involved in regulation of circadian rhythms.

RETINO-GENICULO-CORTICAL PATHWAY

Conscious visual perception is subserved by the primary visual pathway, from the retina to the dorsal **lateral geniculate body** or **nucleus (LGB or LGN)** in the thalamus to the visual cerebral cortex. The remainder of this section will address with this pathway.

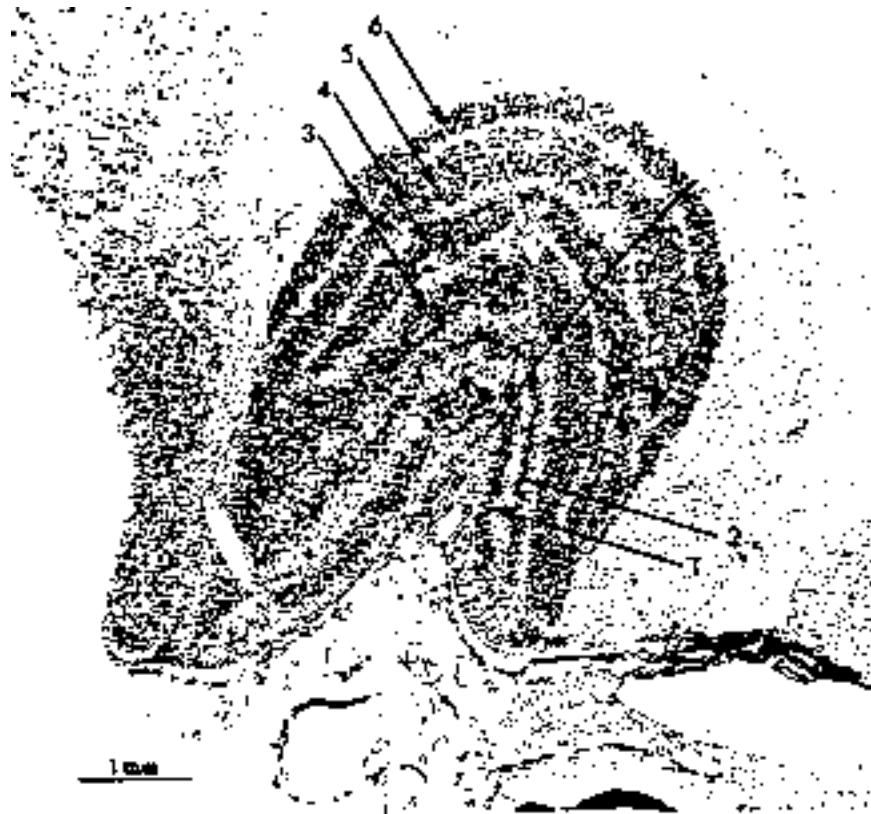
Retinal ganglion cell axons synapse (finally!) on thalamocortical cells in the dorsal lateral geniculate body. As a result of the **partial decussation**, the partial crossing of ganglion cell axons from each eye in the optic chiasm, the axons innervating the LGB on a given side of the brain are derived from the *temporal* retina of the *ipsilateral* eye and the *nasal* retina of the *contralateral* eye. Thus, the ganglion cells that project to the LGB on one side of the brain are stimulated by objects or light coming from the contralateral half of the visual world.



Coronal view of the thalamus, showing the location of the LGB.

Put most simply, the left LGB “sees” the right visual hemi-field, and the right LGB “sees” the left visual hemi-field.

The LGB has six well-defined layers and is innervated in a systematic, topographical fashion, by both eyes. However, axons from the two eyes remain *segregated*. Each layer of LGN cells receives input from one eye only. So, while the LGB receives input from both eyes, single LGB cells are innervated by only a single eye.



Coronal section through the right LGB showing the six layers. Each layer receives input from one eye corresponding to the left visual field. The line drawn orthogonally through the layers passes through cells that are “looking” at the same region in the visual field.

The LGB has several jobs.

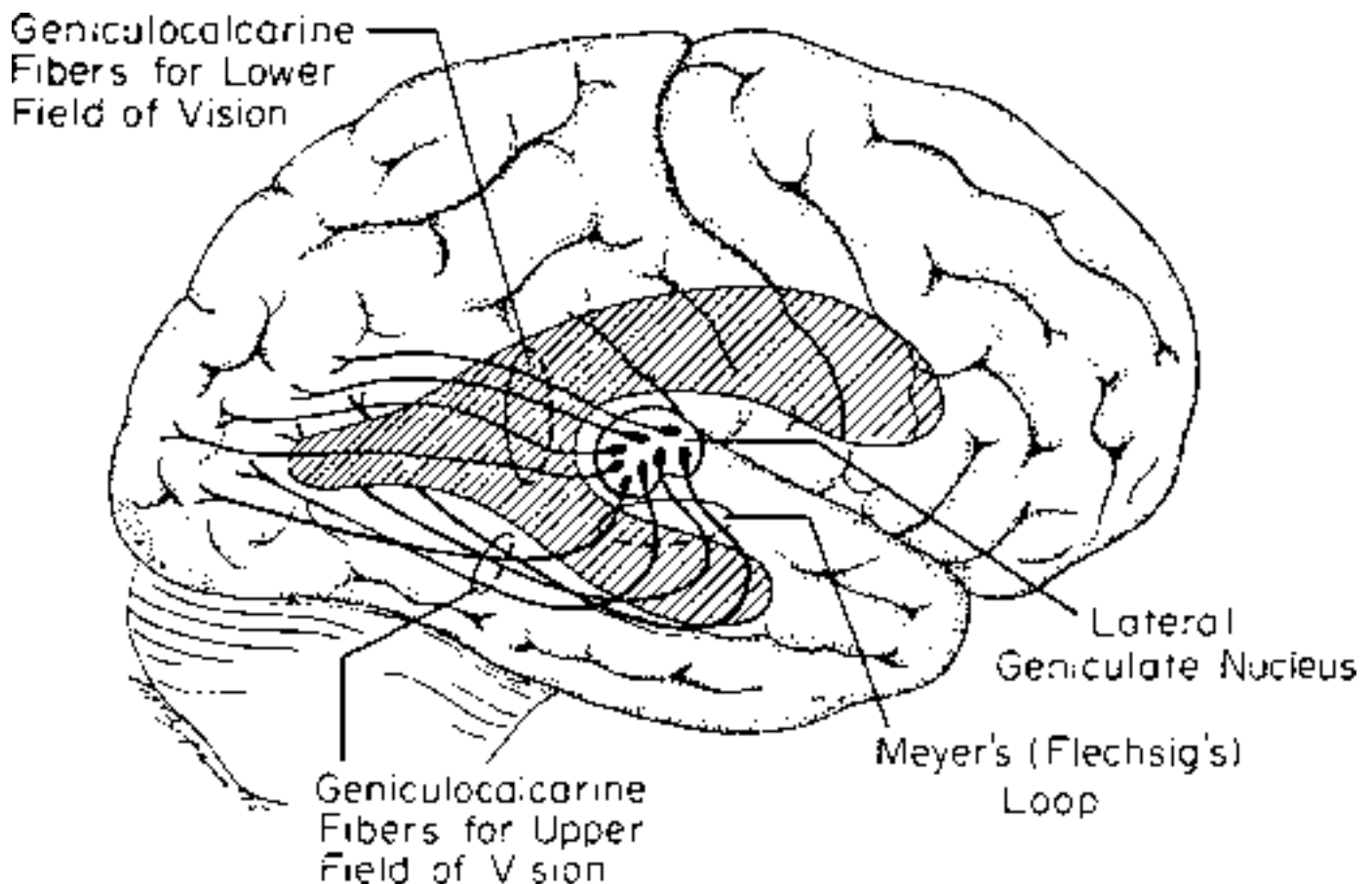
- First, the process of aligning topographically the retinal projections from the two eyes begins in the LGB. There is a complete map of the contralateral visual field in each layer. The six maps are in precise register, and a line drawn normal to the curved layers will pass through cells that map the same visual field location. This precise mapping of the visual field preserves the retinotopic organization and starts to bring corresponding input from the two eyes into register.
- Second, the segregation of visual signals into separate streams destined for different types of visual processing is an important feature of the LGB. Like a cutaneous nerve, the optic nerve contains different functional classes of cells that carry different types of visual information. The different classes of neurons are segregated into different layers within the LGB.
- Third, the visual thalamus acts as a gateway to control the flow and character of the visual signals that reach cortex.

Lateral geniculate body = LGB = The GATEWAY to visual cortex

GENICULOCORTICAL PROJECTION- THROUGH THE OPTIC RADIATIONS

Thalamic neurons in the LGB send their axons to the occipital lobe in cerebral cortex. To get there, the geniculocortical axons travel through the **retrolenticular part of the internal capsule** (the part caudal to the lenticular nucleus), and then through the **optic radiations**.

The optic radiations are retinotopically organized. Geniculocortical axons that map the **lower visual field** travel *directly back* to occipital cortex. In contrast, the axons that map the **upper visual field** swing out *laterally into the temporal lobe* and form an arc called **Meyer's loop**. So, lesions in the temporal lobe can disrupt a specific portion of the primary visual pathways, those related to vision in the upper visual field.



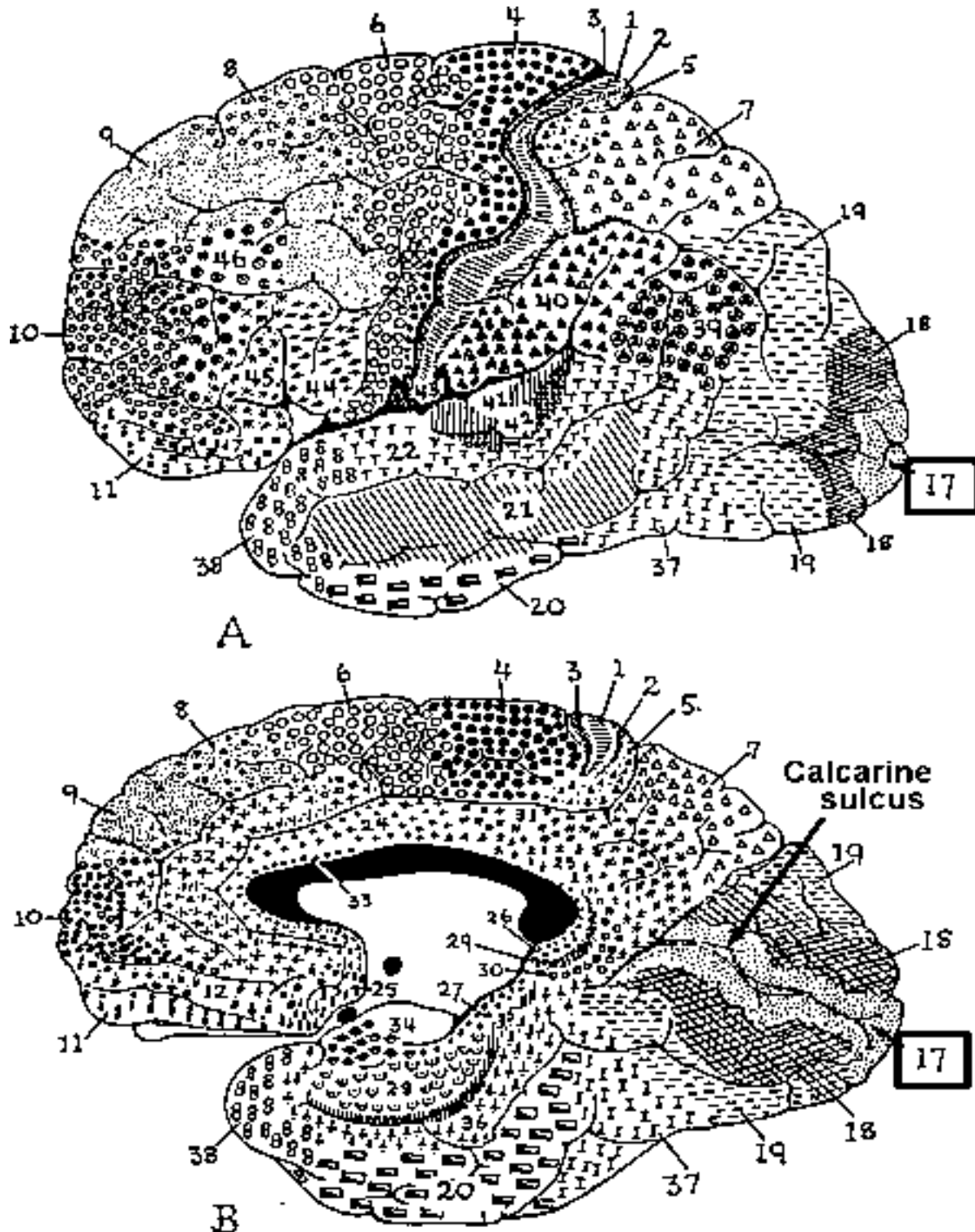
The geniculocortical projection. Lateral geniculate axons mapping the lower visual field project posteriorly to visual cortex. In Meyer's loop, lateral geniculate axons mapping the upper visual field (those destined for the ventral bank of Area 17) swing out laterally into the temporal lobe.

Primary Visual Cortex

The part of visual cortex that receives input directly from the LGB is **primary visual cortex** or **V1** in the **occipital lobe**. To make life fun for medical students, V1 has many other names, each of which you should know. On Brodmann's cytoarchitectural maps, V1 is **area 17**. Area 17 is characterized by a prominent stripe that can be seen with the naked eye, known as the stria of Gennari, after the medical student (!) who first observed it. Thus, area 17 is also referred to as

striate cortex. (The stria is made up of incoming bundles of myelinated fibers from the LGB.) Almost all of striate cortex is confined to the superior and inferior banks of the **calcarine fissure** or **sulcus** on the medial wall of the occipital lobe. Thus, primary visual cortex may also be called **calcarine cortex**.

So, primary visual cortex = V1 = area 17 = striate cortex = calcarine cortex



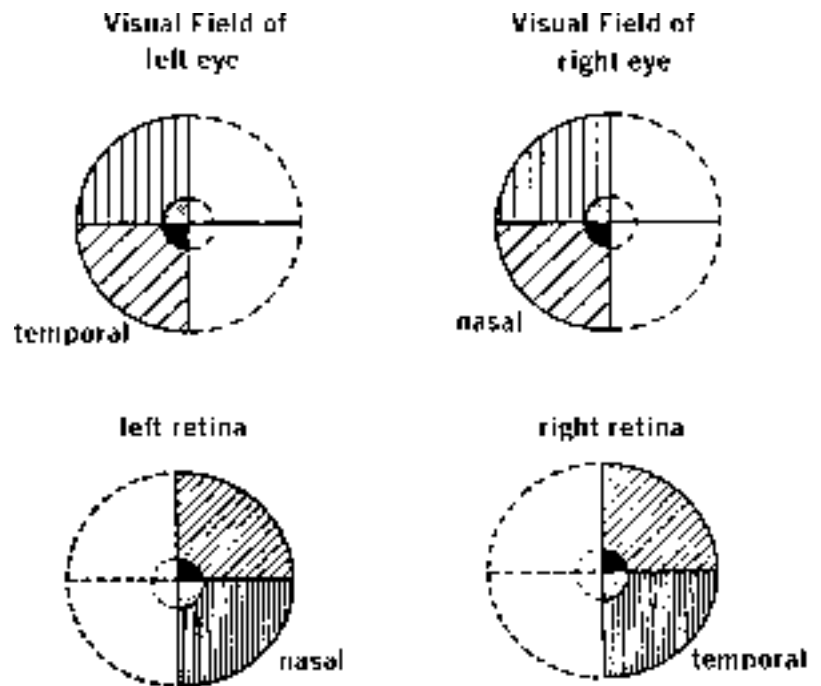
Cytoarchitectural map of human cortex. A: lateral view. B: medial view. Note that area 17 (striate cortex) borders and is embedded in the calcarine sulcus. From Brodmann.

Extrastriate Visual Cortex

Brodmann areas 18 and 19 in the occipital lobe and other cerebral cortical areas concerned with vision are referred to as **secondary visual areas** or **extra-striate cortex**. This includes portions of the occipital, temporal, and parietal lobes. Each of these areas contains a retinotopically organized map of the contralateral visual hemifield.

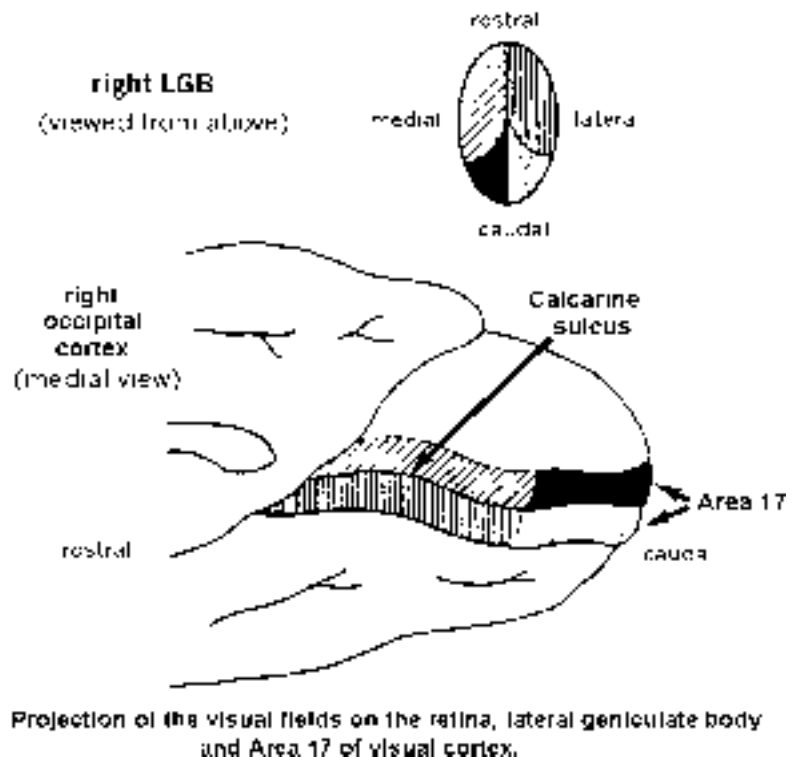
Roughly 25 cortical visual areas have been identified and over half of our cerebral cortex is involved in visual processing. Many of these cortical areas specialize in analyzing a particular aspect of vision, for example, color, form, motion, or spatial relations.

Extrastriate areas compartmentalize visual analyses anatomically, so, for instance, visual area V4 scrutinizes color information while area MT (medial temporal region) analyzes visual motion. Generally, parietal cortical regions appear involved in answering the question “Where is it?” while temporal cortical regions appear involved in answering “What is it?”. Frontal cortex is also involved visually in the production of eye movements.



Organization of primary visual cortex

Area 17 on each side of the brain contains a complete representation of the *contralateral* visual field. This representation is (of course) retinotopically organized. A tremendously enlarged portion of primary visual cortex is devoted to central retinal, or foveal, representation at the posterior pole of occipital cortex. The *upper visual field* is represented on the *ventral bank* of the calcarine fissure (which is innervated by fibers that travel in Meyer’s loop), and the *lower visual field* is represented on the *dorsal bank* of the calcarine fissure.



Blood supply for the central visual structures

Optic nerve: central retinal artery, posterior ciliary arteries

Optic chiasm: anterior cerebral, internal carotid arteries

Optic tract: posterior communicating, anterior choroidal artery

LGB: branches of posterior cerebral artery, anterior choroidal artery

Opt. radiat'ns: branches of ant. choroidal, middle cerebral, and posterior cerebral

Area 17: posterior cerebral, considerable anastomosis with middle cerebral

D. Lesions of the Visual Pathways

Because the visual pathways are organized retinotopically, specific lesions along the visual pathways lead to predictable visual field deficits. This is illustrated in the accompanying diagram.

A) A lesion of one optic nerve results in total blindness in the ipsilateral eye.

B) A lesion at the optic chiasm, as from a pituitary tumor, can interrupt the crossing fibers from both eyes, causing a **bitemporal** or **heteronymous hemianopsia** (or **hemianopia**). (“Bitemporal” because it affects the temporal visual field of both eyes, “heteronymous” because it affects different parts of the visual field in the two eyes, “anopsia” meaning loss of vision, and therefore “hemianopsia” because it affects a visual hemi-field).

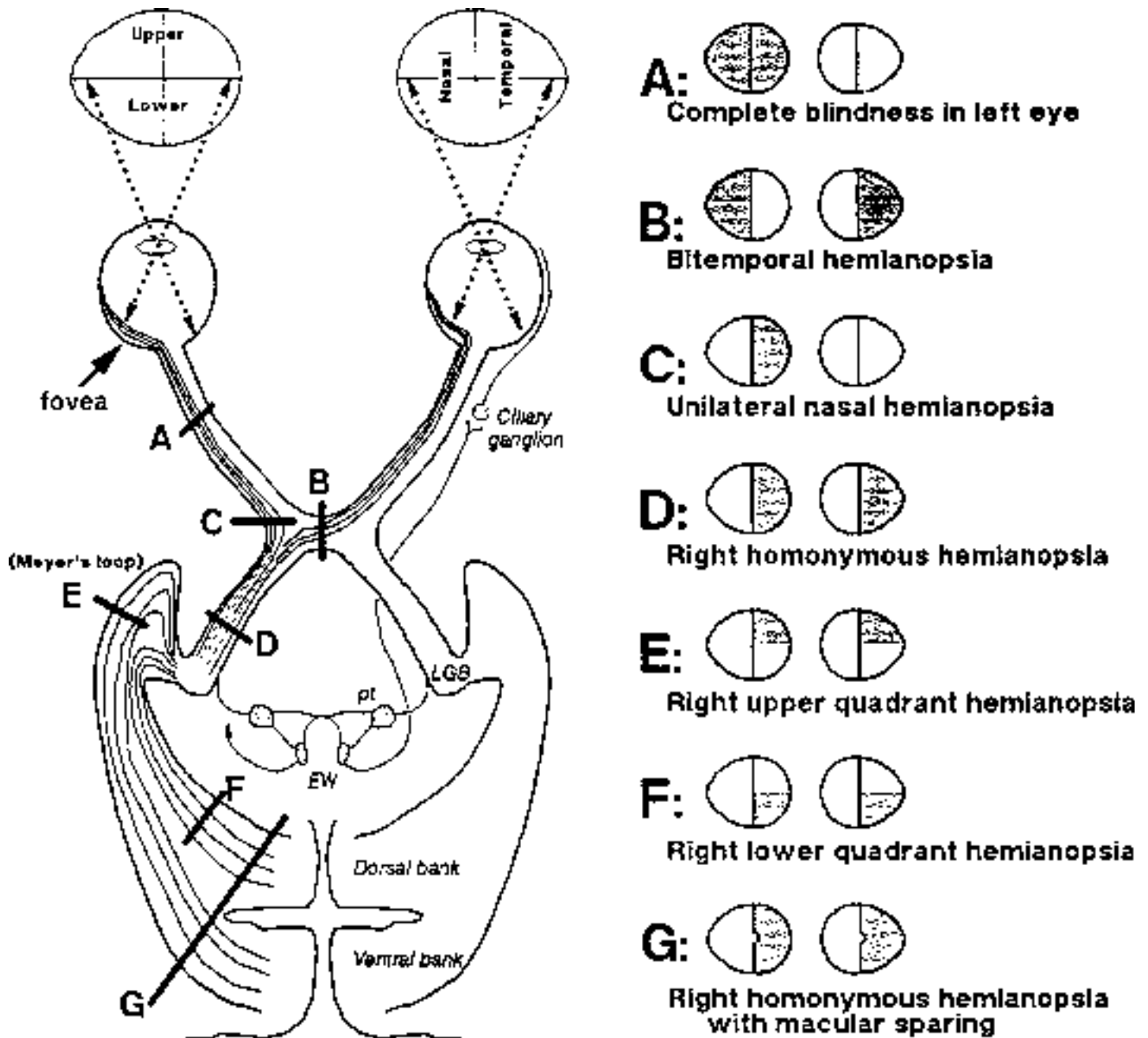
C) Loss of only the ipsilaterally directed axons on one side of the optic chiasm leads to a unilateral nasal hemianopsia. Such a clean lesion is rare.

D) A complete lesion of the optic tract, the LGB, or the entire optic radiations on the left side produces a right **homonymous hemianopsia** (“right” because it affects the right visual field, “homonymous” because it affects corresponding parts of the visual field in both eyes).

E&F) The projection from the LGB to primary visual cortex is by way of the retrolenticular part of the internal capsule and the optic radiations. The fibers enroute to the *dorsal* bank of area 17 travel more or less directly while the fibers enroute to the *ventral* bank swing into the temporal lobe (Meyer’s Loop) before coursing back to the occipital lobe. This explains the specialized visual field defects sometimes seen with temporal lobe lesions. A lesion of just the dorsal-most portion of the optic radiations (F) yields a right **lower quadrant hemianopsia** (or **quadrantanopsia**). A lesion of Meyer’s loop, ventral in the optic radiations, cuts the fibers marked E, resulting in an **upper quadrant hemianopsia** (or **quadrantanopsia**).

G) A lesion in the primary visual cortex (area 17) usually causes **contralateral homonymous hemianopsia**. Curiously, even a large lesion of area 17 on one side of the brain, which produces a homonymous hemianopsia, can leave the macular/foveal region little affected. This poorly understood phenomenon is known as **macular sparing** (remember that the central region around the fovea is called the macula lutea). If both cortices are affected, with macular sparing on both sides, tunnel vision can result.

Lesions affecting just the dorsal bank of the left calcarine fissure result in right lower quadrant hemianopsia. Lesions of the ventral bank result in right upper quadrant hemianopsia.



The effects of lesions at different points along the central visual pathways. Left, diagram of central visual pathways going to the left hemisphere. Letters A-G indicate lesion points. Corresponding monocular visual field diagrams on the right indicate resulting visual deficits. (Remember, the monocular fields for the two eyes will superimpose so that the vertical meridians coincide from the perspective of the binocular patient).

The pathway for the **pupillary light reflex is also included in the diagram. Notice that the pupillary light reflex pathways are entirely subcortical and *unaffected by cortical lesions*. This means that following a cortical lesion that results in perceptual blindness in the visual field, you can still have subcortical visual function.**

SMALL AREA 17 LESIONS

A small lesion in area 17 can produce a scotoma in the visual field. The size and location of the scotoma correspond to the location on the map of the visual field in the calcarine fissure. Such small scotomas are rare (e.g., from gunshot wounds). They are often not noticed by the patients (remember your own blind spot, courtesy of the optic disc?) and found only by detailed visual field testing. Dr. Heatley will talk more about this.

SECONDARY VISUAL AREA LESIONS

Lesions in the visual pathway from the retina to area 17 can produce blindness in some or all of the visual field. In comparison, lesions in extrastriate visual cortex produce more subtle deficits affecting only a particular aspect of vision, rather than eliminating all perception in a specific portion of the visual field. Deficits can occur in visual discrimination of objects, form vision, color perception, and spatial organization, for example.

Lesions in the temporal and parietal lobes may result in higher order cortical processing deficits. For example, bilateral lesions of the inferior temporal lobes result in **prosopagnosia**, the inability to recognize previously familiar faces. Patients can see the face, but can no longer identify it as familiar, even if it is a close family member, or friend. Certain posterior parietal lobe lesions lead to visual **neglect** of objects in the contralateral hemifield. Patients with these lesions may ignore the contralateral half of objects or their own body, for instance thinking that their contralateral (to the lesion) limb belongs to the examiner. In both cases, *other visual functions are preserved*. In sum, lesions in extrastriate cortex do not result in complete perceptual blindness. Rather, the visual deficit affects particular perceptual or cognitive tasks.

CENTRAL VISUAL PATHWAYS: PRACTICE QUESTIONS

1. Which of the following statements about visual fields is **FALSE**?
 - A. an object in the left half of the binocular visual field will be in the nasal visual field of the right eye and the temporal visual field of the left eye
 - B. the lower half of each retina “sees” the upper half of the visual field
 - C. the visual field of the left eye overlaps with a large portion of the visual field of the right eye
 - D. the monocular segments are in the nasal visual fields of each eye
 - E. none of the above

2. Identify the following:
 - A. striate cortex
 - B. retinotopic organization of LGB and visual cortex
 - C. calcarine sulcus
 - D. scotoma
 - E. diplopia
 - F. homonymous hemianopsia
 - G. LGB
 - H. Meyer’s loop
 - I. optic nerve versus optic tract

3. What visual field defects result from lesions at the following sites?
 - A. right optic tract
 - B. right LGB
 - C. left optic nerve
 - D. fibers crossing at the optic chiasm
 - E. Meyer’s loop in left temporal cortex

4. Which of the following statements about the central visual pathways is **TRUE**?
 - A. central to the optic chiasm, the left side of the brain “looks” at the left half of the binocular field of vision
 - B. the LGB projects more heavily to extrastriate cortex than it does to cortical area 17
 - C. lesions in extrastriate visual cortex do not produce complete blindness; the deficits are limited to fairly specific perceptual tasks
 - D. in the visual system, retinotopic organization is seen only at the retina
 - E. two of the above

5. Which of the following lesions and visual field deficits are paired **INCORRECTLY**?
 - A. lesion of the left optic tract - right homonymous hemianopsia.
 - B. small lesion in the upper bank of V1 - small scotoma in the contralateral lower visual field.
 - C. a lesion of Meyer’s loop in the right temporal lobe - left upper quadrant hemianopsia.
 - D. a lesion of the retinal fibers that cross at the optic chiasm - binasal hemianopsia.
 - E. lesion of the right optic nerve - blind in the right eye

6. Which of the following statements about the central visual pathways is/are **TRUE**?
- A. at the optic chiasm, the fibers from the temporal retinae cross, while those from the nasal retinae continue ipsilaterally
 - B. visual thalamocortical fibers are found in the retrolenticular part of the internal capsule
 - C. a single thalamocortical cell in the lateral geniculate body responds well to visual stimulation of either eye
 - D. following a striate cortex lesion on the left, a patient's pupils will not constrict to light shined in the right eye
 - E. neurons in the lateral geniculate nucleus send their axons to the primary visual cortical area in the contralateral occipital cortex

CENTRAL VISUAL PATHWAYS: PRACTICE QUESTIONS ANSWERS

1. D

2. Identifications:

- A. Area 17, primary visual cortex in the occipital lobe.
- B. the preservation in central visual structures of the topographical organization found in the retina wherein adjacent cells "see" adjacent points in visual space.
- C. the location of striate cortex (area 17) on the medial bank of occipital cortex.
- D. a "hole" or blind spot in the visual field
- E. double vision
- F. hemi-visual field defects in the temporal field of one eye and the nasal field of the other (e.g., deficit in the left visual fields of both eyes).
- G. the site in the thalamus where retinal axons synapse on thalamic relay neurons that project to primary visual cortex. A laminated structure, LGB "looks" at the contralateral visual hemi-field and the nucleus as a whole receives input from both eyes, but individual neurons have monocular receptive fields.
- H. formed by the fibers of the optic radiations that dip down into the temporal lobe before swinging back up towards visual cortex - lesions in this region of the temporal lobe produce upper quadrant hemianopsia.
- I. optic nerve - the bundle of retinal ganglion cell axons from the eye to the optic chiasm, contains axons from only one eye.
optic tract - retinal ganglion cell axons running from the optic chiasm to the LGB, contains axons from both eyes.

3. Visual field deficits:

- A. left homonymous hemianopsia
- B. left homonymous hemianopsia
- C. blindness in left eye
- D. bitemporal hemianopsia
- E. right upper quadrant hemianopsia

4. C

5. D

6. B